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THE AMERICAN DERMATOLOGICAL ASSOCIATION

OBLIGATIONS AND OBJECTIVES

C. GUY LANE, M.D.

BOSTON

I extend to every one of the members a cordial welcome to this, the fifth, meeting of this association held in Boston. My appreciation of the honor of presiding over the deliberations of this assembly, with its notable heritage and achievements, I cannot express adequately. The founding of the American Dermatological Association in Philadelphia, sixty years ago, was really the beginning of a fully recognized and independent position of American dermatology, for at that time there were in the field of dermatology no American books, no American research work and no monographs by American authors. The meeting this year coincides with the centennial of the teaching of dermatology in this country, for in 1836 lectures in dermatology were given by Dr. H. D. Bulkley of New York at the Broome Street Infirmary.

At the first annual meeting, in Niagara Falls, N. Y., Dr. James C. White, the first president, greeted the members with these words:

> We assemble now for the first time, prepared to present to each other our views in relation to the general interests of dermatology, to report and discuss the results of our special studies, and to form that more intimate acquaintanceship among ourselves, dermatologists of a wide country, which is so essential to mutual support and understanding.

Dr. White also stated that the Association would be a meeting ground for discussion, that it would furnish opportunity for the study of cutaneous diseases as they occur on this continent and for the establishment of a uniform and simple system of nomenclature and that it would foster the general interest of dermatologists in all its relations to members of the profession and to the public. In the last-mentioned objective Dr. White included medical education to insure proper instruction in dermatology and the establishment of fit hospital accommodations for patients with cutaneous disease. These were the objectives sixty years ago. Can one do better at the present time?

President's Address, read at the Fifty-Ninth Annual Meeting of the American Dermatological Association, Inc., Swampscott, Mass., June 5, 1936.

We members of the American Dermatological Association in this day and age realize how far these objectives, as stated by Dr. White, have approached fulfilment. We are all conscious of the defects which have arisen as educational and scientific progress in our special field has moved forward. We recognize the changing needs from one generation to another. This association has provided a definite continuity, a unanimity of action by bringing its members—us and our predecessors—together so that we could keep pace with the changes which have occurred and could make provisions for the future.

As individual physicians we are all busy with our private practice, our hospital work, our teaching, the various investigations we are carrying on and the many elements of our daily life. As a result we are apt to neglect our obligations to the association, to disregard the actual business matters which concern every society and to overlook—unless one of them affects us directly—the many problems of the day confronting members of the medical profession in general. We all need to review our aims and our obligations occasionally. At this meeting, therefore, may I present for consideration certain affairs of the association in order that we may continue to carry forward the purposes of the association and the objectives so well outlined by Dr. White in 1877, restated by Dr. Hyde in 1898 and amplified by Dr. Stelwagon in 1900?

First of all, I desire to emphasize the need of maintaining close contact with progress in fields outside our own. This association has passed through the period of the recognition of dermatology and syphilology as a legitimate field for specialization. It has progressed beyond the period in which cutaneous manifestations were considered as being in a distinct compartment. It is of course impossible for one to keep abreast of medicine in general in such a way as to be able to bring to bear on a particular problem all the knowledge pertaining to that problem, but this association can furnish us with assistance in the solution of the many borderline problems.

THE CONGRESS

In the first place, I hope that in the near future the association will be able to rejoin the Congress of American Physicians and Surgeons and participate at least once in five years in meetings devoted to general medicine and specialties other than our own. It is my belief that the full value of participation in such meetings has been only partly realized in the past. To me it seems that such a meeting held at intervals provides the opportunity for joint discussions of a borderline topic with some special society which has a field adjacent to ours, and I believe that members of both associations will derive mutual benefit from such discussions.

COOPERATIVE STUDIES

Secondly, the excellent work of the cooperative clinical group in syphilis indicates that it is possible to carry out similar undertakings in other subjects if proper cooperation and funds are available. The association can well stimulate and even sponsor such cooperative clinical committees in pooling their resources in the study of industrial dermatoses, cancer of the skin, tuberculosis of the skin, etc. The benefits to be derived from cooperation are incalculable. Of immediate interest is the report of a committee for the study of industrial dermatoses which was appointed at the meeting of the Section on Dermatology and Syphilology of the American Medical Association in 1935.

The Section on Dermatology and Syphilology at the meeting of the American Medical Association in Kansas City, Mo., in 1936 adopted the report of this committee, which recommended:

1. That the committee continue the study of occupational dermatoses in cooperation with the American Dermatological Association, the Section on Industrial and Preventive Medicine and Public Health of the American Medical Association and the United States Public Health Service.

2. That a "central clearing house" be established for the recording and dissemination of information on industrial dermatoses.

3. That subcommittees be formed in various geographic districts to gather information and report to this central committee.

The incidence of occupational dermatoses, and the losses of time, payment of wages and compensation, etc., require that such a study be carried out in a cooperative way, and if dermatologists do not participate actively it is certain that the program for handling cases of these disorders will be dictated by political lay organizations, insurance companies, state health or labor departments or federal health authorities without regard to the point of view of dermatologists. I believe that we ought to support the work of this committee in every way possible.

SYMPOSIUM

A third means of attack on these marginal subjects is the symposium. In 1902 Dr. George T. Jackson called attention to the value of groups of papers which in the ten preceding years were presented about a special subject assigned for discussion at a meeting. The presentation of three, four or five papers on different phases of one disease or one subject and possibly a comment by an invited guest cannot fail to add something of interest to the knowledge of individual members of the audience. I realize fully the limitations of subjects suitable for discussion in a symposium, but if the subjects and speakers could be selected some time in advance with the idea that definite research work would be undertaken and the literature surveyed such presentations would offer definite progress in a given subject and stimulate further investigation.

The papers on syphilis presented at this session and the discussion amply prove the value of the symposium in our program. Syphilis should always have a prominent place in the programs of this association. That disease is bound to be included in future public health programs, and we should remain in the forefront of the attack on this disease—its diagnosis, its prevention and its treatment. While the cutaneous manifestations of syphilis are said to be vanishing, it is hard to visualize the time when there will not be need of differentiating syphilis from other cutaneous conditions. More attention should be paid to syphilis in dermatologic clinics, and the general knowledge needed in the proper care of syphilis should be amplified in future programs for the training of dermatologists.

MEMBERSHIP

The proposal to increase the limit of membership in the association should receive serious attention. The association has always been a relatively small body and the members have known each other intimately. Of course there are differences of opinion on this point, but in general we have rejoiced in the congenial atmosphere of our meetings. The number of dermatologists in this country has increased greatly, and the limit of membership has been raised from 25 to 40, to 75, to 100 and to 125. It is, however, true that any great enlargement of our membership will tend to lessen the close acquaintance which we have cherished. I am not sure what the ultimate limit of the number of our members should be, but I am sure that the best interests of the association and its members will be served by retaining a relatively small membership. This association now numbers 112 active members; hence urgent action is not required on our membership limit at this meeting. It is possible that the carrying of all members of twenty years' standing in a separate class and the stricter requirements adopted last year concerning attendance and presentation of papers may postpone the need for action on the membership limit for several years. In recent years the desire for opportunities to meet one's neighbors and exchange information has brought about the formation of numerous local societies and dermatologic sections of state medical associations. That there is also a desire for membership in an organization which is more than a purely local society is demonstrated by the fact that several sectional groups have been organized, but there is only one national forum besides the American Dermatological Association, namely, the Section on Dermatology and Syphilology of the American Medical Association. If the interest in our specialty continues, the establishment of another national organization in the field of dermatology may be advisable.

It has been suggested that the members of this association participate in the formation of an American Academy of Dermatology and Syphilology, perhaps patterned along the lines of the American Academy of Ophthalmology and Otolaryngology. This was formed in 1910 with

the purpose of offering to younger men the opportunities of a scientific forum and fellowship. Sections in the various special fields were created; papers were read and discussed, and clinics were held. That organization has over 700 members, and the senior national societies in the different specialties with their prescribed limitations of membership have thrived at the same time. In the last fourteen years the study group or section on postgraduate instruction of the American Academy of Ophthalmology and Otolaryngology has been one of the outstanding activities and most popular features of that organization.

A similar national organization in dermatology with less strict limitations than this association, meeting yearly in the fall, would satisfy a definite demand and eventually serve a valuable educational purpose. Perhaps the time is not yet ripe for the establishment of such an organization, but I believe that the possibility should be seriously considered.

STATISTICS

The reports of the committee on statistics have not received the attention which they deserve. I believe that such reports should be continued and perhaps amplified. Results of treatment, data about one disease and other items could be subjected to statistical study with the members' cooperation. I am aware that many members consider a questionnaire as a nuisance, but the results would be valuable to all concerned. Statistical data furnish evidence not only of the frequency of certain diseases but of the changing incidence as time passes and perhaps of the need of a change in the attitude of physicians toward those diseases. It is to be regretted that so few members have participated in these surveys. Election to the association and acceptance of membership not only should be considered an honor but should carry with it a certain sense of responsibility in working with the association toward fulfilling its purposes. I hope that it will be possible to continue making such surveys from time to time.

CLINIC

The clinic held in conjunction with the meeting has been a valuable experience for the members. I have heard it said that the clinical meetings held by various local societies and also by the different regional groups allow sufficient opportunity for the exhibition of rare conditions in dermatology. The clinic conducted in conjunction with the meetings of the association may not be as essential as it was in the early years of the association's existence, but it ought not to be given up entirely. The clinics held at these meetings have always maintained a high standard and stimulated the adequate presentation of cases elsewhere. They have also served as valuable experience for the younger men and for the men in the smaller communities. It is possible that some other method or methods can be elaborated for the purpose of continuing the clinical features in connection with the meetings of the association.

EXHIBIT

At the meeting of this association an exhibit has been an extremely minor matter, while the exhibit held at the meeting of the American Medical Association has always been well attended and has called forth many expressions of commendation. The custom of having at least an exhibit from the reader of each paper should be developed. Such a display of data should not detract from a paper but should round out to a considerable degree the paper in question by providing a more complete exposition of a subject than can be given in the allotted fifteen or twenty minutes of actual presentation. The discussion of a paper is often continued during the displaying of an exhibit with benefit to all concerned. I realize fully that greater effort is required, on the part both of the exhibitor and of the local committee, in the presentation of the exhibits, but the educational value of a well planned and well executed exhibit cannot be denied.

FINANCES

The report of the treasurer shows that the financial structure of the association is sound. The accumulative feature of small amounts of money is well shown by the present resources. A transfer to the permanent fund of money not immediately necessary has been recommended by the board of directors and is advisable. Furthermore, any action on dues should be based on the accumulation of a small yearly surplus to be added to the permanent fund so that the amount of income at the disposal of the research aid committee would be gradually increased. It may be argued that the dues should be used simply for the ordinary expenses of the association, but the members could well take pride in the advances resulting from the collective aid furnished by means of a research aid fund. The purpose of the association, as stated in the by-laws, is the promotion of the study of dermatology and syphilology in all their relations. The work and influence of this organization can be greatly extended if the association has at its disposal a fund for the purpose of bestowing awards for work well done or encouraging scientific dermatologic contributions by means of grants for such work.

It is time that a real attempt be made to create an adequate research aid fund from within or from without the association or from both. I believe that the research aid committee should be granted the power to raise funds to initiate a program of research work; these funds may not be adequate at first, but they would constitute at least a beginning of the participation of the association as such in active research work. A fund of $50,000 would make it possible for the association to sponsor a fellowship for a full time man or for two or more part

time men devoting their study to problems of interest to us all. Such a fund would be under the control of the association and be used for dermatologic research. It could therefore not be transferred to any other purposes. The funds left to a university or hospital have a mysterious way of not being used always as intended.

GRADUATE TRAINING

Another obligation of the association is to aid in providing adequate training for young dermatologists. In 1881 Dr. James Nevins Hyde stated before the members of this association that a common error in vogue at that time was that the ". . . . study of diseases of the skin was the pursuit of a narrow specialty and that there was an ignorance of the functions and maladies of important internal organs"; he also stated that ". . . . he who would especially devote himself to the investigation of disorders of the skin required the amplest preparation in a finished general medical education and experience."

The standards of yesterday grow into the standards of today. In accordance with the urge of progress, the Advisory Board of Medical Specialties and the Council on Medical Education have adopted somewhat higher requirements for a certificate in a specialty, which are to become effective in 1938. All the special boards have among their purposes the improvement of the standards of practice, and this elevation of the requirements is a logical feature of an attempt to improve those standards. This has been done with the full realization that it is not advisable to raise any standards or regulations abruptly to such an extent as to nullify the objects aimed at. In 1938 and thereafter in order to be eligible to take an examination of a specialty board a candidate after an internship of one year will be required to complete a three year period of study in clinics, hospitals and laboratories which bear the approval of the specialty board and of the Council on Medical Education and Hospitals of the American Medical Association. This period of study is to include an active experience of eighteen months in such institutions and adequate graduate training in the basic sciences pertinent to the specialty. Two years of further study or practice is required before examination. Examinations will be required in the basic sciences as well as in the laboratory and public health phases of the specialty.

No one doubts the value of a background of fundamental or basic science relating to the specialty. There may be differences of opinion on subjects to be classed as basic and the time allotted to each. It would seem necessary that some fundamental work be given in embryology, physiology, chemistry and bacteriology as related to the skin. Histopathology has already been largely developed, and mycology and serology are receiving adequate attention in many institutions. Pharma-

cology, immunology, hematology, endocrinology and the physics of radiology and physical therapy certainly deserve adequate emphasis in the preparation of any person intending to specialize in dermatology.

For such a minimum basic course in science the schedule, as it has been tentatively planned by the American Board of Dermatology and Syphilology, there is allotted about two hundred and fifty hours. An eight month college year provides about twelve hundred hours; hence the suggested schedule for basic work in science would occupy less than 25 per cent of a college year. This schedule could be completed in perhaps three months of the first year, or it could be extended over the whole year, coincidently with the clinical experience. Another matter under discussion is the allotting of six months in a two year residency for basic work, with the expectation that the resident will major in one of the basic sciences during this period. It is of course open to question whether it is desirable to allot a certain number of hours for each subject or whether it is best to define carefully the field to be covered in each subject, indicating its limits and allowing the details for covering the field adequately to be worked out by the individual institution and the head of the department.

The adequate fulfilment of these requirements is an objective of major interest to every member of this association. Not only does the American Dermatological Association act as sponsor for the board, but among its 123 members are the heads of dermatologic departments and dermatologic teaching staffs of all the large institutions. Eighty per cent of the members hold professorial rank, and there are only a few members who do not hold, or have not held, teaching positions. We are all, therefore, vitally interested in a program which is to become effective in 1938, or, if the opportunities are not available at that time, in 1940.

It may be that two years is sufficient, but all will agree that three full years of continuous training will provide a more comprehensive foundation. It is probable that three years, portions of which are spent at different times and at different institutions, will be accepted, provided that the equivalent of three full years of training is maintained.

Concerning the approval of clinics or institutions, it is probable that the board will have a higher standard so far as this specialty is concerned than that determined by the Council on Medical Education and Hospitals of the American Medical Association, at least at the present time. Provision for the inspection of various institutions in order to estimate their capacity for adequate training will undoubtedly be necessary and is certainly advisable, but no machinery for this function is as yet available. As the years pass an adequate guide to the value of training received in the various institutions will accumulate in the records

made by graduates of these different hospitals and medical schools in the examinations by the board.

It is probably not of primary importance whether this specialty training shall center about a clinic or a medical school. The basic science study as a rule can be carried out better in the medical school, but undoubtedly some of the larger departments of dermatology can provide the requisite basic training within the department. Clinics, of course, will furnish the greater part of the teaching as at present, but it will be necessary that the medical schools and the clinics cooperate in providing the necessary facilities.

Three years ago a study of the diplomates who had passed the board examination showed that 75 per cent obtained their training by graduate work through residencies in dermatologic departments or by acting as assistants in offices of well known dermatologists. The other 25 per cent obtained their dermatologic training by clinical experience.

In the three years of training as suggested not only must there be adequate clinical experience and actual supervised instruction in cutaneous diseases and syphilis, but adequate time and facilities must be available for students who are research minded and properly equipped to pursue individual problems as far as possible. In other words, provision must be made for two classes of students, (1) for those who will become teachers and research workers and make for progress in dermatology and (2) for those who desire only to become good practitioners in dermatology.

A training of this kind will furnish an excellent background for the two years of practice or study which will be required before the budding specialist can present himself for examination and obtain full recognition as a specialist in dermatology and syphilology. I have no recommendation to make concerning this program, but I desire the members to be informed of the progress which is being made toward an objective in which all of us are interested.

This problem of placing specialization on a rational graduate basis is one of the important problems facing us at the present time, and our active efforts toward its solution will result in better training of dermatologists, who can go further than we have in solving problems of etiology, in controlling and preventing disease and in providing more rational treatment for patients with cutaneous disease. Such a forward step will redound greatly to American dermatology.

The objectives for which we as members of the American Dermatological Association are striving should ever remain on the high plane established by our predecessors, and in order to attain this ideal we must keep faith with our obligation to the society in order to create the obligations of the association to us as members.

PRURITUS AND HYPERESTHESIA CAUSED BY PARTIAL SENSORY DENERVATION

EXPERIMENTAL ALOPECIA—A CONTRIBUTION TO THE STUDY OF ALOPECIA AREATA

ENRIQUE A. AUBRUN, M.D.
Medical Assistant, Dermatosyphilographic Clinic of the Medical School, University of Buenos Aires, Hospital Ramos Mejía
BUENOS AIRES, ARGENTINA

In 1933 Beeson and Pickett [1] published a contribution to the experimental study of alopecia areata.

In spite of having read my publications [2] in which I conclusively demonstrated the physiopathologic mechanism of the cutaneous lesion obtained experimentally, the authors confined themselves to repeating on twenty-one cats Max Joseph's operation, the extirpation of the second rachidian ganglion with its corresponding roots. Their conclusions were as vague as those of Joseph, who stated in 1886 that the lesions of alopecia obtained by this operation are similar to those of alopecia areata in human patients, which gives the false impression that the nerve section causes the appearance of the disease in the animal. Besides this, they did not study the physiopathologic process leading to the experimental production of the lesions.

Without meaning to be controversial, I think it useful to publish this paper, because I feel that Beeson and Pickett, in spite of the industry which their work implies, have taken a step back in the elucidation of the mystery which shrouds the pathogenesis of alopecia areata.

Among the theories put forward to explain the origin of the disease, without doubt the most promising was that which presupposed the possibility of reproducing it in animals by section or extirpation of certain nerve roots. Max Joseph was the first to practice the ablation of the second cervical rachidian ganglion and its corresponding roots, obtaining patches of alopecia, which he said resembled pelade in human patients and which were interpreted as trophic lesions caused by section of a nerve with a specific trophic function.

From the Institute of Physiology, Medical School, University of Buenos Aires (Prof. B. A. Houssay).

1. Beeson, B. B., and Pickett, W. J.: Experimental Alopecia: A Contribution to the Study of Alopecia Areata, Arch. Dermat. & Syph. **28**:53 (July) 1933.

2. Aubrun, E. A.: (*a*) Pelada experimental de Max Joseph (prurito e hiperestesia por sección nerviosa), Buenos Aires, Imprenta López, 1931, vol. 1, p. 666; (*b*) Pelada experimental de Max Joseph (Prurito e hiperestesia por sección nerviosa), Rev. argent. de dermatosifil. **15**:73, 1931.

These experiments were much discussed and have been the cause of violent disagreement. They have been repeated by many investigators—Mibelli, Samuel, Behrend, Bechterew, Moskalenko and Gregoriantz, Köster, Fay and Wright—some of whom denied the appearance of cutaneous lesions, while others obtained them but gave various explanations for the phenomenon.

The problem was at this stage when I returned to the aforementioned experiments and succeeded in proving that the cutaneous lesions obtained are exclusively due to trauma by scratching, which is provoked by the pruritus and hyperesthesia caused by the partial denervation of the cervicofacial region in the animal.

One hundred and eighteen experiments were made on the second cervical nerve, establishing the fact that section of the sensory tracts of that nerve in the cat produces hyperesthesia or initial pruritus and afterward the appearance of alopecia or of ulceration in the second dermatome, in the region of the skin innervated by the cut root, especially in the areas overlapping the innervation by neighboring nerves (third cervical and trigeminal). The occurrence of lesions is exceptional if ether is used as an anesthetic (4.83 per cent) but more frequent if a dextrose derivative of chloral is used (35.29 per cent). In another series of thirty-six animals, unilateral section of the first three cervical nerves was performed, and under these conditions the degree of pruritus and the frequency of alopecia and ulceration in the second dermatome or root territory of the skin increased (50 per cent).

In order to demonstrate the traumatic origin of the lesions I repeated this experiment in fourteen animals, the heads of which were protected permanently by leather caps. None of them acquired the slightest cutaneous lesion, but the caps showed evident marks of scratching. For further confirmation, when the cap was removed from one of the animals thirty-seven days after the operation, I was able to observe immediate violent scratching, which led to the rapid appearance of alopecia and ulceration.

The pruritus and hyperesthesia are of peripheral origin and appear only in the areas of common innervation between the sectioned nerves and the neighboring untouched nerves, the latter carrying the abnormal sensations to the nerve centers. This can be proved by cutting all three cervical nerves and the trigeminal nerve (which participates in the innervation of the area under observation) of the same side, which prevents the development of the pruritus and the traumatic lesions.[3]

3. By cutting the trigeminal nerve (with or without the cervical nerves), in addition to the classic lesions described, ulcerated pruriginous traumatic lesions, similar to those under discussion, may be produced in a different area (the preauricular, which is also innervated by the cutaneous branch of the vagus nerve).

In later experiments [4] I also showed that extirpation of the cervical sympathetic ganglions does not produce pruritus, cutaneous lesions or lesions in the hair and that sympathectomy previous to the extirpation of the cervical roots does not modify the hyperesthesia and pruritus caused by the operation itself. The sensory alteration does not appear to be due to vasomotor changes or to the increase of permeability of the capillaries.

To summarize, I have clearly shown that the cutaneous lesions, the traumatic origin of which is undeniable, obtained in cats by section of certain nerves do not reproduce experimentally the lesions of alopecia areata, the etiology and pathogenesis of which are still unknown to me.

The practical result of my investigations was the demonstration of the existence of a new type of sensory alteration—the hyperesthesia and pruritus of peripheral origin associated with partial sensory denervation in some cutaneous areas. It remained to give an explanation for the occurrence of the pruritus, that is, to investigate the factor which produces the abnormal sensation in the areas with a common innervation by the sectioned and untouched nerves, the latter forming the efferent path to the nerve center, with the resultant reflex scratching.

In connection with this I wrote in my thesis: [5] "The immediate appearance and periodic intensification which we have observed on several occasions lead us to suspect the existence of some local change which at the present moment we are unable to determine (metabolites)."

Thus I was inclined from the first to suspect that section of the nerve caused some substance to be liberated in the area supplied by that nerve which might cause the described phenomena. For technical reasons I have been unable to demonstrate this hypothesis, though I still consider it the only admissible explanation in the present state of knowledge.

In support of this theory I may say that the analysis of a series of works on general or special physiology during the last few years showed that the idea is gaining ground that the appearance of many physiologic and pathologic phenomena in which nerves have a leading rôle is due to the liberation of substances at a given moment. I confine myself to citing such instances as bear on my own problem.

De Waele, Vandevelde and Braye [6] held that the peripheral vasodilatation observed during excitation of a posterior root is caused by antidromic propagation of the stimulus to the skin, whence, either by

4. Aubrun, E. A.: Prurito e hiperestesia por sección nerviosa: Acción vascular y simpática en el prurito por desnervación sensitiva parcial, Rev. argent. de dermatosifil. **16**:363, 1932.

5. Aubrun,[2a] p. 255.

6. De Waele; Vandevelde, J., and Braye, L.: L'origine et le trajet des vasodilatateurs des racines postérieures, Bull. Acad. roy. de méd. de Belgique **9**:580, 1929.

anastomosis or by the formation of algogenic substances which spread to the surrounding areas, it ascends by the normal paths of the neighboring nerve roots to the spinal and motor centers.

Foerster [7] observed that pain occurs when the peripheral ends of certain nerves are stimulated, and he expressed the belief that it was due to the transmission of the excitation to the neighboring sensory nerves, through peripheral anastomosis. Feldberg and Schilf [8] accounted for the pain as due to the liberation of a substance "H" (of histamine type), which on spreading through the tissues excites the sensory receptors of the neighboring undivided nerves. The latter theory finds support in the unusual duration of this type of pain.

Finally Kibjakow [9] stated that he had found vasodilator substances, metabolites, of peripheral origin in the veins of the part corresponding to the excited posterior roots.

I hope that some special technic will be devised by which it may be proved that the sensory phenomena under consideration are due to the liberation on section of the nerves of an algogenic substance or one causing pruritus, which by its action on the untouched sensory nerve endings causes reflex scratching.

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7. Foerster, O.: Die Leitungsbahnen des Schmerzgefühls und die chirurgische Behandlung der Schmerzzustände, Berlin, Urban & Schwarzenberg, 1927, p. 20.

8. Feldberg, W., and Schilf, E.: Histamin: Seine Pharmakologie und Bedeutung für die Humoralphysiologie, Berlin, Julius Springer, 1930, p. 457.

9. Kibjakow, A. W.: Zur Frage des Vasodilatations Mechanismus bei der Reizung antidromer Nerven, Arch. f. d. ges. Physiol. **228**:30, 1931.

CERTAIN PHASES OF SULFUR METABOLISM OF THE SKIN

JOSEPH V. KLAUDER, M.D.
AND
HERMAN BROWN, B.S.
PHILADELPHIA

Considerable investigation has been conducted regarding the rôle that sulfhydryl compounds play in the cellular activity of normal and abnormal growth, as a factor in oxidation and reduction and as detoxifying agents. The study herein reported embraces these phases of sulfur metabolism in relation to the physiology of the skin in the normal state, in systemic pathologic states and in diseases of the skin. In previous communications [1] we reported the results of studies and reviewed data showing the important rôle that cystine plays in the formation and development of keratin-containing tissue, especially hair, wool and nails.

Sulfur in the skin exists essentially in organic combination. It is believed that a large portion is in the form of cystine and cysteine. Other known sulfhydryl compounds in the skin are glutathione and methionine.

The total sulfur content of the skin was determined rather than the amount of the individual, naturally occurring sulfhydryl compounds. Determination of the total sulfur content is more accurate and affords a composite picture of all the sulfhydryl compounds. Our purpose in this investigation was to make a general survey of the evidence indicating a disturbance of sulfur metabolism.

METHOD

The total sulfur content of the skin was determined according to the method of Frear [2] and is expressed as the percentage of sulfur of the dry weight of the skin. In the preparation of the specimen of skin only superficial fat was removed, preliminary to the drying operation. No attempt was made to carry out an

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Read at the Ninth International Congress of Dermatology and Syphilology, Budapest, Hungary, Sept. 13, 1935.

From the Research Institute of Cutaneous Medicine and the Philadelphia General Hospital.

1. (*a*) Brown, H., and Klauder, J. V.: Sulphur Content of Hair and of Nails in Abnormal States; Therapeutic Value of Hydrolyzed Wool: I. Hair Arch. Dermat. & Syph. **27**:584 (April) 1933. (*b*) Klauder, J. V., and Brown, H.: Sulphur Content of Hair and of Nails in Abnormal States: II. Nails, ibid. **31**:26 (Jan.) 1935.

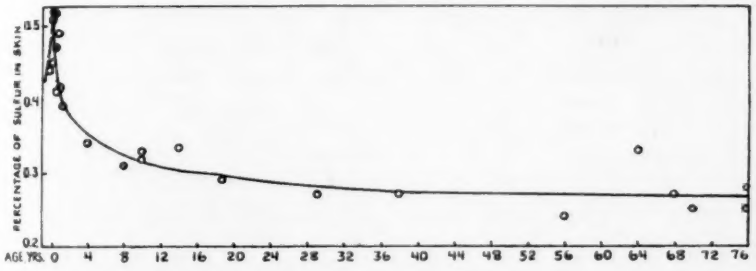
2. Frear, D. E.: The Adaptation of the Benedict-Denis Method to the Determination of Sulphur in Plants, J. Biol. Chem. **86**:285, 1930.

exhaustive series of fat extractions designed to remove cellular lipoids. An estimation of the inorganic sulfur content was of course included in the determination of the total sulfur content. The amount of inorganic sulfur in the skin, however, is insignificant compared with the total amount of organic sulfur. The margin of error inherent in the method employed, we believe, is less than 0.1 per cent. Many of our specimens checked within 0.05 per cent. About 0.2 Gm. of skin as removed from the patient was required for analysis.

The sulfur content of the skin was determined from the following sources: (1) the skin of man from infancy to old age; (2) the skin of rabbits from birth to maturity; (3) the scales and skin of patients with various skin diseases, especially psoriasis; (4) the skin obtained at autopsy from patients with systemic infections or disorders; (5) the skin of mice before and after maintenance on a diet poor in cystine, and (6) slowly and rapidly growing carcinoma in mice and malignant lesions in man.

NORMAL TOTAL SULFUR CONTENT OF THE SKIN

Specimens of normal skin from persons of various ages, from infancy to old age were obtained during life and at autopsy and examined for the total



Curve showing the percentage of the total sulfur content in the skin of man at different ages.

sulfur content. Specimens from patients dying of infections, intoxications and malignant disease were not included in this group. From the results plotted in the chart it can be seen that the sulfur content of the skin decreases with age. During the first year of life the percentage of sulfur in the skin ranges from 0.40 to more than 0.50; it decreases rather abruptly the first few years of life to about 0.35, more slowly until adolescence (from 12 to 16 years), to about 0.30, and thereafter but little or not at all. The normal sulfur content of the skin of the adult appears to be from 0.25 to 0.30 per cent, the majority of the figures being between 0.26 and 0.28 per cent. We are not acquainted with any extensive reports on studies of the percentage of sulfur in normal skin from persons of different ages. Reported analyses embrace the results in one or in a few specimens of normal skin.

For the purpose of comparison, as determined in previous studies,[1] we regarded the normal percentage of sulfur in hair to range from 4.5 to 5.2, and in nails, from 3 to 3.6. In these studies we did not determine if the percentage of sulfur in hair or nails varied from infancy to old age as it does in the skin. In Payne

and Perlzweig's [3] study of the cystine content of nails, no variation on the basis of age was reported. The age range of the patients, however, was from 17 to 70 years.

SULFHYDRYL AS A FACTOR IN NORMAL AND ABNORMAL GROWTH

The skins of litter mates of rabbits were analyzed for total sulfur content from birth to maturity. A series of such analyses were conducted and repeated on a second litter. It was observed that there was a nearly uniform decrease in the total sulfur content from birth to maturity. The following figures for the percentage of sulfur are representative of the results but do not represent the total number of examinations made. In animals up to 2 weeks of age the percentage was about 0.69, decreasing at the age of 3 months to about 0.54; at the age of 8 months it was about 0.46.

In a previous communication [4] we reported the results of a study on the relation of sulfhydryl compounds to abnormal growth (mouse carcinoma). The total sulfur content of different organs of mice maintained on a normal diet and on a diet poor in cystine, the effect of such diet on the rate of growth of cancer in mice and the correlation of the rate of growth of transplanted mouse carcinoma with the sulfur content of such tumors were studied. It was concluded that there was a loss of sulfur in the muscle, liver, spleen, kidney and skin of white mice maintained on a diet poor in cystine, that transplanted tumors grew more slowly in mice maintained on such a diet than in mice on a normal diet, that the rate of growth of mouse carcinoma correlated the sulfur content and that regardless of the factors involved in retarding the rate of growth of the tumors in the animals studied, the sulfur content correlated the rate of growth.

In the study reported here we determined the total sulfur content of benign and malignant lesions involving the skin as well as of malignant tissue involving different viscera in man. The total sulfur content of malignant tissue was compared to the total sulfur content of the normal tissue from which the malignant growth arose. It was observed that benign (nonhairy) melanoma of the skin generally had a high sulfur content. The percentage of sulfur in each specimen examined was as follows: 0.20, 0.39, 0.60, 0.69, 1.05 and 0.29. Malignant melanomas of the skin contained a still greater percentage of sulfur. The percentage in each specimen examined was as follows: 0.50 (surrounding normal skin, 0.27), 1.06, 0.74 and 0.93. Two different specimens of epithelioma of the skin contained 1.2 and 0.81 per cent of sulfur, respectively. A study of the percentage of sulfur in malignant tissue from various viscera did not show uniformly a greater percentage of sulfur than that contained in the organ from which malignant growth arose. Results of the study were not as striking as those obtained in the aforementioned similar study of mouse carcinoma. In the latter study it is to be noted that the animals were exsanguinated prior to examination of different tissue, and hence such tissue was examined free from blood, whereas difficulty was experienced in completely removing blood from specimens obtained from human beings at autopsy.

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3. Payne, S. A., and Perlzweig, W. A.: Cystine Content of Finger Nails in Pellagra, J. Clin. Investigation **12**:899, 1933.

4. Brown, H., and Klauder, J. V.: Total Sulphur of Tissue in Normal and Abnormal Growth (Mouse Carcinoma), J. Lab. & Clin. Med. **20**:1143, 1935.

The skin of ten patients dying of cancer was examined for the total sulfur content. The percentage of sulfur was below normal in four of these specimens, ranging from 0.17 to 0.23; in two it was 0.25 (low normal), and in four it was normal.

Comment.—The conclusion reached in our study that the sulfur content of the skin decreases with age both in rabbits and in man is in accordance with the knowledge of the rôle that sulfhydryl plays as a growth factor. Cystine, the oxidized form of the sulfhydryl-containing amino-acid cysteine, is one of that limited group of amino-acids which is indispensable for normal growth and development. In Thompson and Voegtlin's [5] study of the glutathione content of the organs of the white rat it was observed that the amount of glutathione decreased with the age of the animal. Binet and Magrou [6] made similar observations pertaining to the glutathione content of the liver of rats, and Crosti [7] also found the same to be true of the glutathione content of the skin of rabbits and rats.

Our observation that the rate of growth of mouse carcinoma correlated the sulfur content and that some malignant lesions in man contain more sulfur than the organs in which they arise is likewise in accordance with the knowledge of the rôle that sulfhydryl plays as a growth factor as embraced in the hypothesis of Hammett and his co-workers.[8] Reimann and Hammett [9] have reported gross acceleration of wound healing by the simple external application not only of cystine but also of thiodextrose and thiocresol. Reports of other investigators as to whether malignant tissue contains more glutathione than the surrounding normal tissue have been conflicting.

Our observation of the high total sulfur content of benign and malignant melanoma is in accordance with the observation of others that some melanins are rich in sulfur. This may have some significance in view of the well known fact that a malignant melanoma is highly malignant.

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5. Thompson, J. V., and Voegtlin, C.: Glutathione Content of Normal Animals, J. Biol. Chem. **70**:793, 1926.

6. Binet, L., and Magrou, J.: Composés du soufre et croissance, Presse méd. **40**:853, 1932.

7. Crosti, A.: Alcune osservazioni sul glutatione nella pelle e su suoi metodi di ricerca, Gior. ital. di dermat. e sif. **73**:1526, 1932.

8. Hammett, F. S.: The Chemical Stimulus Essential for Growth by Increase in Cell Number, Protoplasma **7**:297, 1929. Hammett, F. S., and Reimann, S. P.: Cell Proliferation Response to Sulphydryl in Mammals, J. Exper. Med. **50**:445, 1929.

9. Reimann, S. P., and Hammett, F. S.: Cell Proliferation Response to Sulphydryl in Man, Proc. Soc. Exper. Biol. & Med. **27**:20, 1929.

TOTAL SULFUR CONTENT OF THE SKIN OF PATIENTS WITH SYSTEMIC INFECTIONS AND DISORDERS

Skin removed at autopsy from ten patients dying of pulmonary tuberculosis was examined. The percentage of sulfur in seven specimens was low, ranging from 0.21 to 0.24, whereas it was normal in the remaining three. The results of this study are shown in table 1.

The skin of ten patients dying of chronic or acute infection was likewise examined. Chronic infection embraced bacterial endocarditis; acute infection embraced chiefly pneumonia, acute appendicitis and acute meningitis. The percentage of sulfur was low in three specimens (0.21, 0.24 and 0.39, the last being the percentage obtained in an infant aged 1 year) and low normal (0.25 and 0.26) in two. In the remaining five specimens the percentage of sulfur was normal. The skin of twelve patients dying of diabetes mellitus, or its complication, showed a normal range of percentage of sulfur.

TABLE 1.—*Low Percentage of Sulfur in the Skin of Patients Dying of Pulmonary Tuberculosis*

Case	Sex	Color	Age	Postmortem Diagnosis	Percentage of Sulfur of Dry Weight of Skin
1	M	W	56	Pulmonary tuberculosis	0.24
2	F	C	21	Miliary tuberculosis, chronic ulceration	0.28
3	F	W	26	Tuberculosis; pneumonia; diabetes	0.21
4	F	C	30	Diffuse ulcerative pulmonary tuberculosis; tuberculous ulcerations of intestines	0.23
5	F	C	20	Tuberculous bronchopneumonia	0.24
6	M	W	50	Pulmonary tuberculosis cavitation with bronchopneumonia	0.27
7	F	W	34	Fibrocaseous pulmonary tuberculosis	0.24
8	F	C	22	Pulmonary tuberculosis	0.24
9	F	C	21	Chronic ulcerative pulmonary tuberculosis, tuberculous enteritis and peritonitis	0.26
10	M	W	51	Bilateral pulmonary tuberculosis with miliary spread	0.24

In this group was included the skin of four patients with pellagra, all of whom had cutaneous manifestations; the disease in two was severe. The percentage of sulfur in three of these specimens was low and low normal, 0.22, 0.25, 0.26 and 0.29.

The percentage of sulfur in the skin of four patients with arsphenamine dermatitis and one patient with dermatitis due to the ingestion of a gold compound was definitely low, ranging from 0.20 to 0.22.

Comment.—Our findings of a low and low normal sulfur content of the skin in one half of our series of patients dying of acute and chronic infections and in the majority of those dying of tuberculosis is in accordance with our knowledge that sulfur metabolism plays a defensive rôle and that cystine and glutathione are important detoxifying substances.

In studies of Robin and Bournigault [10] it was observed that the total sulfur content was decreased in tissues considerably involved by tuberculosis.

10. Robin, A., and Bournigault, A.: Le soufre dans le foie cancéreux, Bull. Acad. de méd., Paris **83**:178, 1920.

To explain the presence of a low percentage of sulfur in the skin of patients with systemic infections, carcinoma and other chronic systemic disorders it would be desirable to correlate such findings with the results of studies of sulfur balance. Evidence has been reported of a disturbance of sulfur metabolism during fever and in cancer and tuberculosis.

Sullivan and Hess [11] noted a decrease in the cystine content of the nails of patients with arthritis and attributed this to the demands made on the organism for sulfur as a detoxifying agent. In Payne and Perlzweig's [3] study it was observed that the cystine content of nails was decreased in patients with pellagra who presented a severe dermatitis. It is to be recalled that evidence has been submitted (Camurri,[12] Koch and Voegtlin [13] and Smith [14] that the metabolism of sulfur is abnormal in pellagra, and Sabry [15] has reported favorable results in the treatment of this disease with sodium thiosulfate.

In a previous study [1b] on the total sulfur content of nails we reported a low percentage of sulfur in the nails of patients with chronic pulmonary tuberculosis, chronic arthritis of the deforming type, pernicious anemia, inoperable carcinoma and pellagra and of patients with prolonged fever secondary to systemic infection.

Our observations of a definitely low percentage of sulfur in the skin of three patients with arsphenamine dermatitis is in line with the observations reported by Voegtlin, Dyer and Leonard.[16] In their studies experimental evidence was presented indicating that the action of arsenic on protoplasm is essentially due to an action on certain organic sulfur compounds containing sulfur in the mercaptan (sulfhydryl) form. This conclusion was based on the following facts: 1. Arsenic tri-oxide and its organic derivatives readily combine in vitro with hydrogen sulfide or certain sulfhydryl compounds with the formation of condensation

11. Sullivan, M. X., and Hess, W. C.: Studies on the Biochemistry of the Cystine Content of Purified Proteins, Pub. Health Rep., supp. 86, 1930, p. 1.

12. Camurri, V. L.: Atti d. Cong. pellagrol. ital., 1910, p. 67; cited by Kahn, M., and Goodrich, F. G.: Sulphur Metabolism, Philadelphia, Lea & Febiger, 1926.

13. Koch, M. L., and Voegtlin, C.: Chemical Changes in the Central Nervous System as a Result of Restricted Vegetable Diet: II. Chemical Changes in the Central Nervous System in Pellagra, Bulletin 103, United States Public Health Service, Hygienic Laboratory, 1916.

14. Smith, J. H.: The Influence of Solar Rays on Metabolism, Arch. Int. Med. **48**:907 (Nov.) 1931.

15. Sabry, I.: Ueber die chemische Natur des Pellagratoxins und die Entdeckung der Thiosulfatbehandlung der Pellagra, Dermat. Wchnschr. **96**:265, 1933.

16. Voegtlin, C.; Dyer, H. A., and Leonard, C. S.: On the Specificity of the So-Called Arsenic Receptor in the Higher Animals, J. Pharmacol. & Exper. Therap. **25**:297, 1925; The Mechanism of the Action of Arsenic upon Protoplasm, Pub. Health Rep. **38**:1882, 1923.

products. 2. All protoplasm with an active metabolism contains sulfhydryl compounds, as indicated by a positive nitroprusside test. 3. The toxic action of arsenoxide on trypanosomes in test tube suspensions and in the living rat can be completely inhibited by supplying an extra amount of certain sulfhydryl compounds (cysteine, thioglycollic acid, glutathione, glycylcysteine and thiosalicylic acid). 4. The toxic action of arsenoxide on rats is diminished by a previous injection of thioglycollate, as shown by the fact that these animals survived longer than the controls that received arsenic only.

Voegtlin and Thompson [17] have shown that the arsenic of arsenoxide is tenaciously retained by the body of the albino rat and that the drug disappears fairly rapidly from the blood, which is evidence that the arsenoxide has a great affinity for tissues. As Voegtlin points out, as in the case of trypanosomes, it seems probable that glutathione or some other sulfhydryl compounds of the tissues might react with arsenoxide, and this, of course, would reduce the amount of such compounds in the tissues to such an extent that they would be injured. In our study the low sulfur content of the skin of patients with arsphenamine dermatitis gave the lowest values obtained in the entire study. This low sulfur content is doubtless the result of demands made on the organism for sulfur, which Voegtlin and his co-workers have shown plays an important rôle as a detoxifying agent in arsenical poisoning.

It is interesting to note that in Voegtlin, Dyer and Leonard's study sodium thiosulfate failed to show a detoxifying power for arsenoxide as did the sulfhydryl compounds tested, especially reduced glutathione. They failed, therefore, to offer an experimental explanation of the common use of sodium thiosulfate in the treatment of arsenical poisoning. They suggested that intravenous injections of glutathione be employed. Since glutathione is difficult to obtain, Voegtlin, Dyer and Leonard thought that it might be possible to secure a beneficial effect by increasing the cystine-glutamic acid content of the patient's diet, since the toxicity of arsenic was reduced if the animal was fed a mixture of glutamic acid and cystine.[18]

17. Voegtlin, C., and Thompson, J. V.: Quantitative Studies in Chemotherapy: VI. Rate of Excretion of Arsenicals a Factor Governing Toxicity and Parasiticidal Action, J. Pharmacol. & Exper. Therap. **20**:85, 1922.

18. These experiments suggest that proteins should not be withheld in the treatment of patients with toxicologic reactions to arsenic. In such patients and also in those with toxicologic reactions to gold compounds, we administer, in addition to sodium thiosulfate, 10 Gm. of glutamic acid daily and cystine, which may be obtained by the free ingestion of yolk of eggs. Cystine can be administered cheaply as hydrolyzed wool, which contains 1.5 Gm. per thirty-two cubic centimeters. Our studies [18a] suggest that cystine in hydrolyzed wool is in the form of laevo-cystine.

In experiments on toxicity in rats, Voegtlin, Johnson and Dyer [19] demonstrated that cystine, cysteine and glutathione detoxified cyanide; sodium thiosulfate and thioglycollic acid also offered protection. They expressed the belief that cyanide reacts chemically with the cystine and glutathione of the body and that detoxification can essentially be attributed to the restoration of the proper physiologic concentration of these compounds in the tissues by the addition of an extra supply of sulfur from without.

From the foregoing data and in view of our findings of a low percentage of sulfur in the skin and nails of persons with systemic infections and disorders it appears that the skin acts as a depot of sulfur on which demands are made as part of the defensive mechanism operative in infections and intoxications. Apparently sulfur in organic combination, especially compounds containing the sulfhydryl radical or divalent sulfur, act as detoxifying agents, although there is evidence that sulfur compounds not existing normally in the organism, sodium thiosulfate for example, may furnish sulfur in an active form.

Voegtlin, Dyer and Leonard's employment of sulfhydryl compounds and their suggestions as to diet are pertinent in the treatment of other intoxications and of systemic infections.

It is possible that determination of the sulfur content of the skin or, what is more practical, of the nails, if it is shown that the percentage of sulfur in the nails correlates that in the skin, may be of practical value in the study of some systemic infections, intoxications, cutaneous diseases and pathologic states and may furnish clues as to sulfur therapy.

TOTAL SULFUR CONTENT OF THE SKIN OF PATIENTS WITH VARIOUS DISEASES OF THE SKIN

A total of thirty-nine examinations were made of the sulfur content of the skin or scales or both of thirty-three patients with disease of the skin, eleven different diseases being represented.

It was observed that the percentage of sulfur in scales from skin in which the percentage of sulfur was normal (from 0.25 to 0.30) ranged from about 0.68 to about 0.80. The percentage of sulfur in scales varied from two and one-half to two and three-fourths the amount contained in the skin. The percentage of sulfur in the skin can therefore be approximated from the percentage in the scales.

The sulfur content was within normal limits in the skin of from one to three patients with the following diseases: generalized eczema, syphilis (secondary stage), lichen planus, pemphigus (estimated from scales), diffuse seborrheic dermatitis (psoriasiform type), sycosis vulgaris and pyoderma and of eight patients with dermatitis exfoliativa. The percentage of sulfur was low (0.22) in one patient with lupus vulgaris and low normal in one patient with sarcoid of

19. Voegtlin, C.; Johnson, J. M., and Dyer, H. A.: Biological Significance of Cystine and Glutathione: I. On the Mechanism of the Cyanide Action, J. Pharmacol. & Exper. Therap. **27**:465, 1926.

Boeck with pulmonary tuberculosis; it was normal in another patient with the same disease with pulmonary involvement. In two patients with disseminated neurodermatid (prurigo of Besnier) the percentage of sulfur was high (0.34 and 0.45 at the age of about 20). Of seven adults with lupus erythematosus the percentage of sulfur was definitely high (0.35, 0.36, 0.40 and 0.47) in four; it was normal in two and low in the remaining one.

Comment.—The tendency for the sulfur content to be low in the skin of patients with lupus vulgaris and sarcoid of Boeck is in accordance with our observations of a low percentage of sulfur in the skin and nails of patients with pulmonary tuberculosis.

The presence of a high percentage of sulfur in four of six patients with lupus erythematosus is consistent with the results of the studies of Crosti,[7] in which it was observed that the amount of glutathione was increased in the skin of one patient with lupus erythematosus. It is difficult to interpret the significance of these observations. They are in contrast to the presence of a low percentage of sulfur in patients with pulmonary tuberculosis and to the tendency for low values in patients with chronic systemic infections.

Ward [20] and others have shown that cystine is the only aliphatic amino-acid of the protein complex which has any marked absorption for solar ultraviolet rays. The capacity of cystine to absorb solar ultraviolet rays is much greater than that of any of the known aliphatic compounds. This power is as great for lesser wavelengths as that of phenylaminopropionic acid, which has the cyclic phenyl group in its molecule. It appears, therefore, that the protective action of keratin-containing tissue against ultraviolet rays is due to its cystine complexes.

In a previous study,[1b] we therefore determined the sulfur (cystine) content of the nails of four patients sensitized to the sun. The results were negative; the percentage of sulfur was normal.

It is to be noted that the percentage of sulfur, as presently discussed, is uniformly high in the skin of patients with psoriasis, which disease is benefited by exposure to the sun, whereas the percentage of sulfur is high in lupus erythematosus, which disease is adversely affected by sunlight; the percentage tends to be low in pellagra, which disease is likewise adversely affected by sunlight. From these data it does not appear that sulfur metabolism of the skin is concerned in the pathogenesis of sensitization to the sun.

Although further studies are being conducted on the percentage of sulfur in the skin of patients with chronic pyogenic infections of the skin, it is interesting to note that the percentage of sulfur was normal in two patients with sycosis vulgaris and in one patient with chronic

20. Ward, F. W.: The Possible Ring Structure of Cystine, Biochem. J. **17**: 898, 1923.

pyoderma. These normal findings offer no explanation for a lack of the defensive rôle that sulfur may play in the pathogenesis of chronic pyogenic infections of the skin. The findings are in contrast to the tendency toward low sulfur values in the skin of patients with systemic infections.

PERCENTAGE OF SULFUR IN THE SKIN OF PATIENTS WITH PSORIASIS

Thirty-two patients with psoriasis were examined. A total of forty analyses was made of the percentage of sulfur in the scales, the uninvolved skin of the

TABLE 2.—*Percentage of Sulfur in the Skin at the Site of Psoriasis, in the Uninvolved Skin of Patients with Psoriasis and in the Skin After Disappearance of Psoriasis*

Case	Sex	Age	Stage of Disease	Duration, Years	Percentage of Sulfur		
					Uninvolved Skin	Involved Skin	Skin After Disappearance of Psoriasis
1	F	46	Acute; generalized	20	....	0.52	....
2	M	26	Acute; severe; generalized	10	....	0.44, 0.53*	0.34
3	F	48	Scattered patches on extremities	40	0.36	0.38	0.39†
4	F	73	Chronic; few patches	20	....	0.49	....
5	M	71	Chronic; few patches	10	0.39	....	....
6	M	42	Acute; many patches	15	....	0.38	0.33
7	F	53	Chronic; scattered patches	6	0.39	0.50	....
8	M	29	Chronic; scattered patches	6	0.39	0.44	....
9	M	34	Acute; many patches	10	0.45	0.48	....
10	M	42	Subacute; many patches	..	0.37	....	0.34
11	F	46	Chronic; few patches	20	....	0.42	....
12	F	65	Chronic; few patches	2	0.34	....	....
13	M	40	Acute; many patches	18	0.36	....	....
14	M	54	Acute; generalized	20	....	....	0.39
15	M	66	Chronic; patches on legs and scalp	20	....	....	0.43
16	M	38	Few mild lesions on trunk	7	....	....	0.37
17	M	67	Inactive; mild; scattered patches.	21	....	0.44‡	0.46
18	M	54	Acute; generalized	20	....	....	0.39
19	F	40	Acute; generalized	20	....	0.45	....
20	M	53	Chronic; few lesions	13	0.33§	....	....
21	M	64	Chronic; scattered patches	27	....	0.34	....
22	F	35	Chronic; scattered patches	10	....	0.38	....
23	M	21	Chronic; scalp	2	....	....	0.33

* Percentage of sulfur after eighteen injections of liver extract.
† Percentage of sulfur after twelve injections of liver extract.
‡ Percentage of sulfur on a diet low in protein.
§ The patient had arthritis; the percentage of sulfur in the nails was 2.39.

patients with psoriasis, the skin at the site of psoriasis or the skin after the disappearance of the disease. A combination of these examinations was made on some of the patients. The ages of the patients ranged from 10 to 71 years.

In all cases except two an abnormally high percentage of sulfur was present in uninvolved skin, in skin involved by psoriasis and in skin after the disappearance of the disease. In the two exceptions the percentage of sulfur in the uninvolved skin of one patient was 0.28 (normal) and in the uninvolved skin of another patient, 0.31 (high normal). The data for these patients are omitted from table 2.

Generally it was observed that the skin at the site of psoriasis contained a greater percentage of sulfur than the uninvolved skin and that after the disappearance of the disease the percentage of sulfur decreased to an amount approximating that found in the uninvolved skin during psoriasis (see table 2). For example, the average percentage of sulfur in the uninvolved skin of eight adults with psoriasis was 0.37, whereas in the skin of eight patients at the site of psoriasis it was 0.44 and in the skin of eight patients after the disappearance of psoriasis it was 0.38. For comparison, we regard the normal range of the percentage of sulfur in the skin of adults to be from 0.25 to 0.30.

The highest percentages of sulfur in the group of specimens from patients with psoriasis, indeed, in all specimens in the entire study, were present in the uninvolved skin of two children. The percentage of sulfur in one child, aged 10 years, was 0.71, and in the other, aged 15 years, 0.56. The data on these patients are omitted in table 2. These high percentages can doubtless be correlated with the age of the patients. As stated previously, the normal range of percentage of sulfur in the skin of children is higher than that in the skin of adults. In one other child, aged 10 years (from the group of patients with psoriasis), the percentage of sulfur in the uninvolved skin was 0.42, which is low in comparison with that found in the skin of the other two children. This child was the only patient in the group with psoriasis who had an associated pyoderma. It is to be noted that many writers have commented on the rarity of pyogenic infections of the skin in patients with psoriasis. The high percentage of sulfur in the skin of patients with psoriasis should be considered in explanation of the infrequent association of pyoderma and psoriasis.

The patients in cases 2 and 3 (table 2) were treated with injections of liver extract, such injections being without apparent effect. In one patient the skin (psoriasis still present) showed a greater percentage of sulfur after than before the injections of liver extract. In the other patient the percentage of sulfur was the same before and after the liver therapy. The second examination of this patient was made after the disappearance of the psoriasis, which was treated locally.

One patient in the series had arthritis. The uninvolved skin showed a percentage of sulfur of 0.33, which is low in comparison with the percentage found in other patients with psoriasis. The nails of this patient likewise showed a low percentage of sulfur, namely 2.39.

The percentage of sulfur in the scales of patients with psoriasis ranged from 0.78 to over 0.90. These figures are consistent with the high percentage of sulfur in the skin of patients with psoriasis.

Acuteness or chronicity of psoriasis and its resistance to treatment could not be correlated with the percentage of sulfur in the skin. In only a few patients was a high percentage of sulfur (above 0.50) in the skin associated with severity of the disease and its resistance to treatment.

Comment.—Other investigators have reported a high percentage of sulfur in psoriatic scales. Krakow [21] found a percentage of 1.88 as compared with 0.74 in the normal skin of the palm. In Strickler and Adams' [22] analysis of seven specimens the percentage ranged from 0.82

21. Krakow, cited by Joffe.[30]

22. Strickler, A., and Adams, P. D.: The Nitrogen and Sulphur Content of Scales in Psoriasis and Exfoliative Dermatitis, Arch. Dermat. & Syph. **25**:11 (Jan.) 1932.

to 0.95 in six; in the remaining one it was 0.74. Grüneberg [23] reported a high sulfur content in psoriatic scales.

We are not acquainted with any reported study of the percentage of sulfur in the skin of a large number of patients with psoriasis. Grüneberg reported an analysis of the percentage of sulfur in the skin of four patients with psoriasis. In four of five specimens the percentage of sulfur was high, ranging from 0.38 to 0.53. The highest values were obtained in the skin at the site of healing lesions. Grüneberg did not study the skin after the disappearance of the disease. He presumed that the percentage of sulfur is high in the latent stage of psoriasis since it is high in the healing stage. Grüneberg attributed a high sulfur content in the skin of persons with psoriasis to a possible alteration in the function of the cortex of the adrenal gland. One gathers from Grüneberg's report that the therapeusis of psoriasis should be directed toward increasing the sulfur content of the skin. Apparently for this reason Grüneberg treated persons with psoriasis with extract of the adrenal gland, since Kubo has shown that such administration increased the sulfur content of the skin of rats and rabbits. He also employed liver therapy,[24] since Milbradt has shown that administration of liver extract causes an increase of glutathione in the skin.

Our study in which it was observed that the percentage of sulfur in the skin tends to decrease after the disappearance of the disease, yet is still abnormally high, would suggest that the therapeusis of psoriasis should be directed toward decreasing the high percentage of sulfur.

An abnormally high percentage of sulfur in the skin of patients with psoriasis suggests that the metabolism of sulfur is abnormal. There is reported evidence of disturbance of sulfur metabolism in psoriasis, some of which, however, is conflicting. Hämmerli [25] found an increase in the excretion of sulfur, which Geber [26] could not corroborate in his study. Danilevskaja,[27] as well as Levin and Kahn,[28] found an increase in

23. Grüneberg, T.: Mikroanalytische Untersuchungen über den Schwefelgehalt normaler und krankhaft veränderter Haut unter besonderer Berücksichtigung der Psoriasis, Arch. f. Dermat. u. Syph. **168**:183, 1933.

24. Grüneberg, T.: Die Lebertherapie der Psoriasis, Dermat. Wchnschr. **97**: 1793, 1933.

25. Hämmerli, T.: Untersuchungen über den mineralischen Stoffwechsel bei Psoriasis, Monatsh. f. prakt. Dermat. **53**:177, 1911.

26. Geber, H.: Nitrogen und Schwefelstoffwechseluntersuchungen bei Psoriasis vulgaris, Dermat. Ztschr. **20**:377, 1913.

27. Danilevskaja, E.: Anorganischer Schwefel im Blut und Schweiss der Hautkranken, Russk. vestnik dermat. **7**:690, 1929.

28. Levin, O. L., and Kahn, M.: The Chemistry of the Body in Diseases of the Skin, Am. J. M. Sc. **162**:698, 1921.

the nonprotein sulfur content of the blood, and Gallego Burin [29] and others reported a decrease in the glutathione content of the blood. Joffe [30] observed a decrease in the sulfate content of the urine, which increased after improvement of the disease. In an interpretation of high percentage of sulfur in the skin of patients with psoriasis the following considerations are perhaps pertinent. Sulfur compounds, especially glutathione, are essential physiologic tissue constituents concerned in biologic oxidation-reduction phenomena. There is evidence that the pathogenesis of psoriasis concerns the oxidation-reduction mechanism of the epithelial cell, a view championed by Van Kerkhoff.[31]

On the basis of our findings we favor the use of a diet with a low protein content in therapy for psoriasis, as advocated by Schamberg, but do not find liver therapy of value. It is difficult to correlate our findings with the beneficial effects of a diet poor in fat and evidence of a disturbance of fat metabolism in psoriasis, as reported by Grütz and Bürger.[32]

SUMMARY

The total sulfur content of the skin was determined according to the method of Frear and is expressed as percentage of sulfur.

The sulfur content of the skin was determined from the following sources: (1) the skin of man from infancy to old age; (2) the skin of rabbits from birth to maturity; (3) the scales and skin of patients with various cutaneous diseases, especially psoriasis; (4) the skin obtained at autopsy on patients with systemic infections or disorders, and (5) slowly and rapidly growing carcinoma in mice and malignant lesions in man.

Sulfur in the skin exists essentially in organic combination. It is believed that a large portion is in the form of cystine and cysteine.

The sulfur content of the skin decreases with age both in rabbits and in man. The normal percentage of sulfur in the skin of infants ranges from 0.40 to 0.50; it decreases the first few years of life to about 0.35; at adolescence it is about 0.30 per cent, and in adults it ranges from 0.25 to 0.30 per cent.

The rate of growth of mouse carcinoma correlated the sulfur content. The sulfur content of benign (nonhairy) melanoma of the skin

29. Gallego Burin, M.: Glutathion y psoriasis, Actas dermo-sif. **26**:373 (Feb.) 1934.

30. Joffe, M.: Sulphate Metabolism in Psoriasis, Urol. & Cutan. Rev. **38**:261, 1934.

31. Van Kerkhoff, J. H. P.: Beiträge zur Kenntnis der Psoriasis vulgaris und ihrer Behandlung, Leipzig, S. Hirzel, 1929.

32. Grütz, O., and Bürger, M.: Die Psoriasis als Stoffwechselproblem, Klin. Wchnschr. **12**:373, 1933.

was generally high. Malignant melanomas of the skin contained a still greater percentage of sulfur. The sulfur content of malignant tissue from various viscera did not show uniformly a greater percentage of sulfur than that contained in the organ from which malignant growth arose.

The sulfur content of the skin was low and low normal in one half of the series of patients dying of acute and chronic infections and in the majority of patients dying of tuberculosis. The sulfur content of the skin of persons with pellagra was low and low normal. It was uniformly low in the skin of patients with arsphenamine dermatitis.

The sulfur content of scales varied from two and one-half to two and three-fourths the amount contained in the skin.

Of twelve different cutaneous diseases in which the sulfur content of the skin was examined, there was a tendency toward a low value in lupus vulgaris and sarcoid of Boeck; the content was high in four of seven patients with lupus erythematosus and uniformly high in patients with psoriasis. The percentage of sulfur was abnormally high in the skin at the site of psoriasis, in the uninvolved skin and in the skin after the disappearance of the disease. As a rule the skin at the site of psoriasis contained a greater percentage of sulfur than the uninvolved skin, and after the disappearance of the disease the percentage of sulfur decreased, approximating that of the uninvolved skin during psoriasis.

The significance of these findings is discussed with reference to: the rôle that sulfhydryl compounds play in cellular activity of normal and abnormal growth and the rôle that sulfur plays in the defensive mechanism. It appears that the skin acts as a depot of sulfur on which demands are made in infections and intoxications. The evidence of altered metabolism of sulfur in psoriasis is also considered.

1934 Spruce Street.

2101 Pine Street.

TRYPARSAMIDE

A FURTHER QUESTIONING OF THE ALLEGED NONSPIROCHETICIDAL PROPERTIES OF THE PENTAVALENT ARSENICAL IN TREATMENT OF HUMAN SYPHILIS, WITH A SUGGESTION REGARDING ITS READOPTION INTO THE CURRICULUM OF THERAPY FOR EARLY SYPHILIS

H. SUTHERLAND CAMPBELL, M.D.
LOS ANGELES

The pentavalent arsenical compound tryparsamide, as synthesized by Jacobs and Heidelberger, was produced at the Rockefeller Institute in 1917. It possesses the following structure: the sodium salt of normo-phenylglycinamide-para-arsonic acid, containing 25.32 per cent arsenic in pentavalent form. It is a white crystalline powder, colorless and odorless in water, in which it is readily soluble. Early experimental inquiry demonstrated that the tolerance of different animal species for it varied widely, that the toxic effects were confined to doses close to the minimal lethal dose, which was distinctly high, and that recovery from a sublethal dose was peculiarly rapid and complete. Several persons reported most favorable results from its use in treatment of trypanosomiasis in man. This work was followed by a report in 1919 by Brown and Pearce, who studied a large series of animals that were infected with various strains of trypanosomes and spirochetes. They noticed that there was no organic or functional disturbance following the administration of a therapeutic dose of tryparsamide and that although the action of the drug in treatment of spirochetal infection was not striking, "a very definite effect is produced upon the course of the infection by treponema pallidum. In the case of blood spirochetes the infection is ameliorated and even though the spirochetes are not immediately destroyed the infection is frequently brought to a termination which leaves the animal in a condition not unlike that produced by more powerful spirocheticidal agents. It does possess a considerable degree of spirocheticidal action, but its chief effect is seen in the peculiar manner in which it modifies or controls the course of the infection."

A further report by Lorenz, Lovenhart, Bleckwenn and Hodges was most enthusiastic regarding the use of tryparsamide in treatment of neurosyphilis. They stated that the use of this drug in therapy of syphilis was based not on its spirocheticidal action, which is comparatively feeble, but on its unusual features: the promptness of recovery of an experimental animal from toxic injury following the use of the drug, the tolerance of the subject to repeated doses of the drug, its

decided tonic effect and its ability to induce resolution and healing of syphilitic lesions, even in the presence of actively motile spirochetes. A clinical study published by Moore, Robinson and Keidel stated that they had used tryparsamide in treatment of the various types of syphilis occurring in man. From their results in treating eight patients with early syphilis, one of whom had primary involvement, they concluded that the drug is contraindicated at this stage of the disease because of its feeble spirocheticidal activity. In twenty-four cases of late syphilis they found therapy with tryparsamide to be inferior to therapy with arsphenamine and stated that it should be used to supplement treatment with mercury and arsphenamine, not to supplant it. A later report by Moore, Robinson and Lyman, dated Sept. 20, 1924, gave conclusions based on the treatment of one hundred and thirty-three patients with neurosyphilis. They stated that in primary and secondary syphilis or in tertiary syphilis unaccompanied by neurosyphilis, the improvement after tryparsamide therapy was so slight that its further use in treatment of these infections was precluded. In this group ten cases of "primary and secondary syphilis" were cited in which the dose of tryparsamide was as high as 7 Gm. but failed to heal the lesions. No indication of the number of cases of primary syphilis was given. It was also stated that the most striking clinical results were obtained from treating patients with meningovascular involvement. Pearce and Brown [1] intimated that their results were similar to but more favorable than those of Moore and his associates. Healing of lesions was hastened by tryparsamide therapy, and the Wassermann reaction of the blood became almost negative. They treated "a few patients showing indolent or regressive primary and secondary lesions with distinctly favorable effect. A few patients with active primary or secondary lesions were subsequently treated. The lesions were unaffected or the activity so increased that the drug was discontinued." No definite statement was made regarding the number of cases in this series. Neither was mention made of the number of primary lesions treated. As a result of these early findings, work on the effect of tryparsamide therapy in man was confined almost exclusively to the action of the drug in the treatment of neurosyphilis. One somewhat divergent and later observation by Futaki is of interest. He noted that in a case of rat bite fever in man due to Spirochaeta morsus-muris, the primary sore healed as rapidly with the use of tryparsamide as with the use of arsphenamine. On the other hand, there was little or no effect on other secondary cutaneous lesions and no beneficial action on the course of fever. Soloman, Epstein and Burke suggested that there were stimulation and healing of local tissue from the use of tryparsamide without

1. Pearce, L., and Brown, W. H.: New York State J. Med. **24**:751, 1924.

destruction of the blood-borne spirochetes. A great deal of animal experimentation with this drug concerning the following factors has been performed: the minimum lethal dose, the arsenic content of blood following its use, the mode of its excretion and its ability to penetrate into the spinal canal. To a lesser degree the latter three phases have been studied in relation to the effect of the drug in treatment of human beings. As is typical of research on syphilis, opposite opinions were voiced. For instance, Voegtlin, Smith, Dyer and Thompson demonstrated that tryparsamide possesses to a high degree the ability to penetrate into the central nervous system; on the other hand, Fordyce and Meyers stated that tryparsamide does not possess unusual penetrative power. The history of tryparsamide is interesting, and the drug holds an enviable position in the present armamentarium against syphilis. At the outset, however, it was subjected to no small degree of criticism, and it suffered the vicissitudes common to so many new compounds recommended for use in the therapy of syphilis. It appears that the early pessimism accorded the action of the drug, including its use solely in the therapy of neurosyphilis, was due to observations made over too short a time. As the years passed, the judgment became more favorable, until today tryparsamide is considered by many authorities to be equal to malaria therapy for the treatment of neurosyphilis. It is true that the production of toxic amblyopia in a relatively small proportion of patients treated with tryparsamide has been of sufficient moment again to cause the value of this drug to be questioned. It is interesting that while some observers stated the belief that involvement of the optic nerve does not obtain in animals following the use of tryparsamide, more recently Young and Lovenhart demonstrated that the toxic effect of the arsenicals on the optic nerve is distinctly related to the molecular structure of the compounds and that arsenicals with the amino group in a para position to the arsenic, such as atoxyl and tryparsamide, produce optic lesions in rabbits, while arsenicals with the amino group in a meta or ortho position to the arsenic, such as arsphenamine or neoarsphenamine, are totally harmless. Without doubt tryparsamide is the safest of the arsenicals to use in the absence of an involvement of the eyegrounds. The presence of this condition may be accurately determined before instituting therapy by an examination of the eyes and a check of the visual fields. The objectionable reactions which may occur from the use of tryparsamide when certain precautions are not taken do not usually obtain until four or five injections have been given; the consensus indicates that after an unfavorable reaction has occurred the patient should not again be subjected to the drug, even after a rest cure.

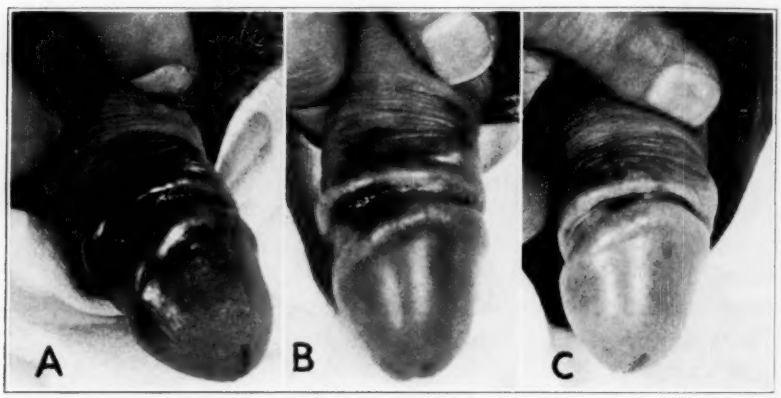
With the exception of the comparatively few instances of toxic amblyopia that have occurred from the use of tryparsamide, objectionable immediate and late reactions common to the other arsenicals are

absent. This fact, as well as its action in general, is decidedly paradoxical and difficult to understand when it is remembered that the arsenical content of the average dose is high, being approximately from 240 to 700 mg. It should be recognized that beyond the assumption that the drug is a "stimulator of resistance" and a "penetrator of nerve tissue" the mechanism of its action is unknown. One must accept the evidence that whereas the use of tryparsamide in the treatment of primary, secondary and tertiary syphilis other than involvement of the nervous system is followed by somewhat mediocre results, its use in the therapy of neurosyphilis has given results far superior to those produced by any other drug that is employed in the treatment of this condition.

Although the older experimenters found that the use of tryparsamide in the treatment of early syphilis was unwarranted because it affected only a few lesions and fresh lesions often appeared in spite of heavy doses, not one denied that the drug had some spirocheticidal activity. Today, however, the contention is common that tryparsamide possesses no spirocheticidal properties and that therefore its use in the therapy of neurosyphilis should be supplemented by the use of arsenicals possessing spirocheticidal properties. This statement is made despite the fact that many experienced earlier reporters contended that they obtained better results in treating neurosyphilis with tryparsamide alone than with it in combination with other metals. For these reasons and because of the paucity of research on the action of tryparsamide on primary syphilis and, also, because I believed that the contention that the drug totally lacks spirocheticidal properties is neither scientific nor justified in the light of former experience, I used tryparsamide again in treating primary syphilis. Those who declaim this procedure as unnecessary because of the vast amount of animal research performed with tryparsamide must recognize that while the results of animal experimentation are usually helpful, they are not applicable in the strictest sense to man. Most animal experimentation with a drug is based on determining the curative dose, i. e., that single dose which will neutralize a recent infection in an animal. The status of cure is judged by the healing of lesions, the disappearance of spirochetes or the fact that negative results follow the transplanting of a gland from the infected animal to a healthy one. In treating the disease in man, it is impossible to administer a single curative dose of any drug. The major toxic reactions common to man do not occur in animals; furthermore, certain physiologic reactions differ widely in animals and in man; for example, the best therapeutic index for arsphenamine in animals is from 1 to 12, and the best for neoarsphenamine is 1 to 25; these values indicate that the action of neoarsphenamine is superior to that of arsphenamine, whereas for man the preponderance of evidence indicates that the reverse obtains.

The first case observed was that of a patient with a chancre of approximately four days' duration. He had received no local medication. The intravenous injection of 2 Gm. of tryparsamide was followed by no visible manifestation of healing. Twenty-four hours after therapy, a slight enlargement of the lesion occurred, not a Herxheimer reaction but merely the advance in the cycle which one might expect without therapy at this stage. Dark-field examination revealed living spirochetes. I instituted neoarsphenamine therapy and used a smaller dose than usual at first because of the pentavalent arsenic already given. This early change of therapy was made because I am mindful of and fully concur with Pusey's dictum concerning the golden value of the early therapeutic hours.

The second case came to my attention more recently: A young man of approximately 24 years of age presented a chancre of about three weeks' duration. Local medication had been used but had been discontinued in disgust four days previously, as the lesion steadily became worse. Examination by dark field gave positive results; the Wassermann test of the blood showed a 3 plus reaction; there was localized adenitis but no sore throat, headache or rash. Figure *A* was taken on



A, photograph taken on Sept. 17, 1935, before treatment was instituted. *B*, photograph taken on September 19, forty-eight hours after 2 Gm. of tryparsamide had been administered. *C*, photograph taken on September 23, six days after therapy with tryparsamide was started.

Sept. 17, 1935. The patient was given 2 Gm. of tryparsamide intravenously; on the next day there was definite evidence of healing and only a slight manifestation of a localized reaction of the Herxheimer type. Approximately twenty-four hours after institution of tryparsamide therapy systematic dark-field search of many fields revealed only 2 spirochetes. Forty-eight hours after therapy was started, no spirochetes could be noted in numerous searches. Figure *B* was taken on Sept. 19, 1935. On September 21 3 Gm. of tryparsamide was given. Figure *C*, taken two days later, on Sept. 23, 1935, illustrates the degree of clinical change that occurred six days after the institution of tryparsamide therapy. The chancre was entirely healed ten days after the first dose of tryparsamide.

It becomes evident that in some cases and under certain conditions tryparsamide is definitely spirocheticidal in man. It is interesting that this small series of cases corroborates the former observations of Pearce,

who found that an early chancre was unaffected or even aggravated by tryparsamide therapy while healing of an older chancre was definitely stimulated by its use. I should like to emphasize the fact that although the evidence of repair shown in figure *B*, taken forty-eight hours after the institution of tryparsamide therapy, is perfectly clear, it does little justice to the physical change observed. Indeed, the evidence of immediate healing was equaled only by the numerical reduction and diminished activity of the remaining spirochetes. Experiments were conducted to determine the action of tryparsamide on the living, shortly isolated, spirochete. Fields were obtained showing many motile spirochetes; a dilution of tryparsamide equal to the average hematogenous dilution in the human being was made. This was allowed to permeate the fields by capillarity. The organisms ceased all movement within a few minutes, many of them showing distorted angulation. These tests proved to be entirely useless, as the use of physiologic solution of sodium chloride or even sterile water caused the same phenomena, i. e., the early loss of motility of the spirochetes and their distortion. Perhaps the sudden alteration of temperature or of concentration may be the occasioning factor, but no conclusion has yet been reached regarding these peculiar reactions.

It may be stated that the contention that tryparsamide lacks spirocheticidal properties is without foundation in fact, and the assertion that better results are obtained in the treatment of neurosyphilis when tryparsamide is supplemented by other arsenicals cannot yet be universally accepted as statements to the contrary have been made by several persons of unquestioned experience. Furthermore, it cannot be denied that there is difficulty in understanding why a drug like neoarsphenamine, which fails over an adequate period to check the degenerative clinical phenomena of neurosyphilis even when supported by various other metal compounds should suddenly acquire merit when used in conjunction with an arsenical of different stucture. Were the condition that of an alternate metallic action an explanation might be acceptable on the basis of the habituation of the organism to a drug, but it seems that one is deprived of that reasoning here, since two arsenicals are being dealt with, and the suggestion of symbiotic action is somewhat unique outside the realm of the micro-organism. Furthermore, if tryparsamide is deprived of all spirocheticidal properties, how can one adequately explain the distinct beneficial clinical results following its singular use in meningovascular syphilis, a condition which can be legitimately classified only as an acute infectious process or the exacerbation due to intense activity of the spirochete? It is commonly admitted that this is the type of neurosyphilis most amenable to therapy with tryparsamide. The purpose of this paper, however, is not only to question the spirocheticidal properties of tryparsamide but largely to

advocate its use as part of the routine treatment of early syphilis. It is generally admitted by the foremost authorities that with the present mode of therapy from 18 to 20 per cent of the patients are modestly labeled as having "inescapable breakdowns"; in other words, they are patients destroyed by the disease; of these, 12 per cent have neurosyphilis. This condition develops in spite of the excellent modern standards of syphilotherapy. It is an accepted fact that von Jauregg, using malaria therapy, demonstrated that many of the persons with neurosyphilis could be reclaimed after having reached a condition of actual degeneration. Other workers, over a period of time, stated that tryparsamide gave equally good results in the process of reclamation. It must be further recognized that certain primary lesions may flourish in the face of either form of therapy. Thus, it will be noted that a close parallel exists between the clinical results obtained by the use either of malaria or of tryparsamide. Is it therefore not logical to believe that a similar parallel exists after the use of either of these agents in the early therapy of syphilis?

Kyrle [2] stated the premise that if malaria was possessed of such beneficial qualities as to be able to reclaim many of those suffering actual degeneration from the ravages of the disease, its action previous to any destruction of the central nervous system should be of far greater benefit. In other words, it should possess the property of prophylaxis. How his perspicacity was rewarded may be gleaned from the report of Matuschka and Rosner, made after his death, five or six years after the institution of his method. The report concerned treatment of two hundred and thirty-two patients and is worthy of recapitulation. The severity of the test is understood only when one recognizes that a single course of treatment was given to each patient. This single course consisted of arsphenamine, malaria and arsphenamine.

	Reaction of Blood to Wassermann Test Before Treatment	Reaction of Blood to Wassermann Test After Treatment		
Duration of Disease	Positive	Negative	Influenced	Uninfluenced
From 1 to 2 years.....	232	230	99.1%	0.9%

In fifty-six of the cases in which the reaction of the spinal fluid had been positive, it became negative. Tests of the blood and of the spinal fluid of the patients continued to give negative results, and the patients showed no clinical evidence of syphilis for five years.

The essential value of this group of cases becomes evident only when it is realized that most early reports on the therapy of syphilis embracing thousands of cases have usually dwindled to a number rarely in excess of that in the series just cited at the end of five years, which is the minimum period of value for judging a cure.

2. Personal communication at the Finger Clinic in Vienna, 1925.

Because of the profound difficulties of administering malaria therapy in the early stages of the disease, with its enforced incapacitation for a longer or shorter time, the main reaction to the foregoing report has been a feverish indulgence in utilizing various methods other than malaria for elevating the temperature of the body, in spite of the fact that von Jauregg, who had had some twenty-five years of previous experience with elevation of body temperature by various methods in the therapy of syphilis, sounded a pessimistic note at the outset, which has apparently been sustained. He persisted in maintaining that biologic reactions other than the effect of raised body heat enter into the reaction equation, which is imperfectly understood.

The success of Kyrle's procedure suggested further evidence in support of the contention that two separate and distinct types of spirochetes exist in the production of the disease. One type is resistant to forms of treatment other than malaria or tryparsamide. Irrespective of theories, it cannot be denied that the utilization of modern continuous alternate metallic therapy in early syphilis has proved inadequate in controlling the condition of 20 per cent of all patients so treated, while early malaria therapy supported by metals has demonstrated beyond question its effectiveness. Because of the difficulty of giving malaria therapy to patients with early stages of syphilis and because a close parallel obtains between the clinical results of therapy with malaria and those of tryparsamide therapy in patients with late degenerative syphilis, I have incorporated tryparsamide into my curriculum of therapy for early syphilis. In other respects the course of treatment closely follows the outline of continuous alternate metallic therapy as given recently by the Cooperative Clinical Group; I shall report on these cases in the future.

SUMMARY

In some instances tryparsamide possesses definite spirocheticidal properties.

The present generally adopted methods of metallic therapy result in the loss of about 20 per cent of the patients treated.

The method of Kyrle, in which malaria is utilized prophylactically in treatment of early syphilis, renders the maximum of good results; that is, 99 per cent of the patients are cured.

As malaria therapy is largely proscribed in the early stages of syphilis for many obvious reasons, the suggestion is made that tryparsamide be incorporated into the regular curriculum of metallic therapy of early syphilis, irrespective of its apparently mediocre value in suppressing early lesions, because its effect so closely parallels that of malaria in the clinical end-results in the therapy of neurosyphilis.

1930 Wilshire Boulevard.

HALO NEVUS

LEUKODERMA CENTRIFUGUM ACQUISITUM (SUTTON); LEUKOPIGMENTARY NEVUS

SAMUEL FELDMAN, M.D.
AND
ISIDORE M. LASHINSKY, M.D.
NEW YORK

In 1916 Sutton reported two cases of a condition which he considered to be an unusual variety of vitiligo, and he named the disease leukoderma centrifugum acquisitum.[1] In one case there was one oval patch, in the exact center of which was a small round elevated brownish maculopapule. It resembled a small pigmented nevus and, according to the statement of the patient, had been there only since the onset of the attack, which dated back three years. There was no hyperpigmented areola surrounding the patch of vitiligo.

The second patient had four lesions which were similar to the one described. Two of the lesions were faint and almost imperceptible; the mother of the patient stated that originally one of these patches was much more distinct but that it had gradually regained some of its color.

On microscopic examination Sutton noted an increase of pigment in the basal layer of the epidermis in the central zone and an infiltration in the cutis of cells which stained deeply with basic dyes, which he interpreted as being of endothelial origin. There was no mention of any change in the white zone.

Sutton's interpretation of the condition in his two cases was based on several considerations. In spite of the fact that he made no mention of it in his paper, one could surmise that he considered the condition as leukoderma because of the mother's statement that one of the patches had regained some of its normal color. One need not emphasize the uselessness of such information for the purpose of making scientific deductions. His further deduction that the condition was acquired was evidently made from a statement in the history that the condition was not present at birth. Even if this is taken for granted, one is not justified in assuming that this disease is acquired in the sense that one may acquire an infection, because it is known that even true nevi may not

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From the Department of Dermatology and Syphilology, Morrisania City Hospital, service of Dr. Samuel Feldman.

1. Sutton, R. L.: An Unusual Variety of Vitiligo (Leukoderma Centrifugum Acquisitum), J. Cutan. Dis. **34**:797, 1916.

appear until later in life. "Centrifugum" in the title was probably meant to indicate a reversal of the so-called *Pigmentverschiebung* so often mentioned in the German literature. It simply expresses changes which occur under certain conditions when the cutaneous pigment disappears or becomes diminished in certain locations and increases in others. In vitiligo this relative increase in pigmentation takes place immediately at the border of the patch. Whether or not the coiners of the term *Pigmentverschiebung* actually thought that the pigment is transferred from the depigmented to the pigmented area by some agent is, of course, hard to determine; however, it seems that that is the impression of some dermatologists. In Sutton's disease the pigment is supposed to be deposited in the center of the lesion instead of at the periphery. For that reason Sutton and a number of others who reported similar cases stressed the lack of a hyperpigmented border in that condition. As a matter of fact, pigment is formed in the melanoblasts of the epidermis and is not transferred there. The rôle of the chromatophores is purely passive. They exert a phagocytic action on the pigment which finds its way to the cutis from the melanoblasts. Furthermore, the pigmentation of the center of the lesion in the condition under discussion is true pigmentation and certainly has nothing to do with *Pigmentverschiebung*.

If one takes it for granted that the central spot is a nevus and at the same time assumes that a hyperpigmented border is essential for a diagnosis of either leukoderma or vitiligo, the condition in the cases described by Sutton and others as instances of leukoderma acquisitum cannot be interpreted as either of those mentioned. It would be more reasonable to interpret the achromic patch as a cutaneous defect in the form of local albinism or as achromia associated with other pathologic and functional changes. On the other hand, the lack of a hyperpigmented border is of doubtful value in the interpretation of these lesions, as at least one case has been reported in which a definite hyperpigmented border was present.

REVIEW OF THE LITERATURE

In reviewing the literature on the subject we noted that Hebra and Kaposi [2] observed the condition as early as 1874. In their textbook of the diseases of the skin, they stated that leukoderma may start near or around a pigmented nevus. In 1910 Sir Humphrey Rolleston [3] reported the case of a patient who had obstructive jaundice due to a carcinoma of the mesentery. This patient had round patches of vitiligo, some of which contained a central mole. The vitiliginous portion was

2. Hebra, F., and Kaposi, M.: Diseases of the Skin, translated by Warren Tay, London, The New Sydenham Society, 1874, vol. 3, p. 180.

3. Rolleston, H. P.: Jaundice, with Area of Unpigmented Skin, Proc. Roy. Soc. Med. (Clin. Sect.) **3**:195, 1910.

jaundiced like the rest of the skin. In 1915 Almkvist [4] presented a patient who had a pigmented nevus with a white halo, the latter having the characteristics of naevus anemicus. In 1917 Shelmire [5] reported the case of a man who had numerous white areas, some of which had a centrally located pigmented spot. He stated that new lesions were forming which had no pigmented central spots. The histologic report was made by J. H. Black, the same pathologist who reported on the pathologic changes in Sutton's cases. That may partly account for the same interpretation of the disease in both instances. In describing the changes in the cutis he stated that there were vascular dilatation and a mild infiltration of round cells. Deeper than the infiltration were large masses of large ovoid cells which showed prominent and deeply staining nuclei. "These cells were apparently endothelial in type." He also stressed the point that there was no hyperpigmentation at the border. When one views the photomicrographs appended to both Sutton's and Shelmire's article, one cannot help being impressed by the fact that there is a fair degree of similarity between this pathologic picture and that of pigmented nevus. In 1918 Bunch [6] presented at a meeting of the Royal Society of Medicine of England a girl 12 years old who had had many patches of vitiligo and two patches of canities on the hairy scalp about one year previously. In three of the patches were deeply pigmented moles. A biopsy specimen of one of the moles showed masses of cells which had a definite arrangement in bundles and contained pigment. These, according to Stogden, who made the biopsy, were probably of endothelial origin. Bunch presented two patients with a similar condition, one in 1919 and one in 1920.

The year 1920 ended the period during which the central nevus was regarded by some as being made up of endothelial cells. Later authors either regarded the central spot as a frank nevus or reported no biopsy.

In 1921 Petges [7] reported a case in which an ordinary pigmented nevus was surrounded by an area of depigmentation, indistinguishable from vitiligo. Nevus cells were found in the pigmented center. In

4. Almkvist: Ein Fall von eigentümlichen Naevi, Dermat. Wchnschr. **60**:74, 1915.

5. Shelmire, J. B.: An Unusual Variety of Vitiligo (Leukoderma Centrifugum Acquisitum), J. Cutan. Dis. **35**:163 (March) 1917.

6. Bunch, J. L.: White Spot Disease and Vitiligo, Brit. J. Dermat. **30**:203, 1918; Vitiligo Patches with Central Pigmented Mole, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **11**:18, 1918; Vitiligo with Central Pigmented Moles, ibid. (Sect. Dermat.) **13**:148, 1919-1920.

7. Petges: Hairy Nevus Surrounded by Vitiligo, Bull. Soc. franç. de dermat. et syph. **6**:302, 1921.

the same year Little [8] reported a case in which there were patches of vitiligo, some of which had a central mole. In 1922 Montpellier [9] reported one case of his own and reviewed eight from the literature.

The first comprehensive paper on the subject was written by Stokes,[10] in 1923. He stated that he observed more than half a dozen cases in which the center of the lesion was clinically and pathologically a nevus. One patient whose condition he described had previously had many moles without any white-ringed lesions. He later acquired about fifty lesions with white halos about them. He did not say that the halos developed around preexisting lesions, but one gains the impression that that is what he meant to imply. He also reported two cases in which there was achromia around pigmented, verrucous and hairy nevi. He found no pigment in the epithelial cells of the epidermis in the white area and no chromatophores in the cutis; hence there was no phagocytic action to explain the process of depigmentation. Stokes expressed the belief that a physical or chemical disturbance in the equilibrium of the affected skin may be responsible for the destruction of pigment and the disappearance of melanoblasts.

In 1924 Weber [11] reported a case in which a central nevus was surrounded by an area of depigmentation. He formulated a law which he called "a law regarding the distribution of depigmented areas when they are superadded to pigmented nevi" and said that when vitiligo of unknown origin occurs in a healthy child, there is a tendency for the vitiligo to surround any mole or nevus that the child may have. That presupposes that in every instance the nevus is the first to appear, the vitiligo being superadded. No one at present would concede the remotest possibility that Weber's postulate might be true, as it is known that nevi without pigmented halos and white patches without central nevi can be found side by side with so-called Sutton's disease in the same patient. Furthermore, it is known that at least in one instance the vitiligo was first to appear, the central nevus developing much later. He presented a girl 8 years old who had patches of typical vitiligo which appeared when she was 7 years old. One of the patches had in its center a miliary raised blackish-brown mole, around which the white patch formed a halo. He asked the question: "Is the achromic patch

8. Little, Graham: Case Report, Proc. Roy. Soc. Med. (Sect. Dermat.) **14**:42, 1921.

9. Montpellier: Leukoderma Appearing Around Pigment Nevi, Bull. Soc. franç. de dermat. et syph. **29**:81, 1922.

10. Stokes, J. H.: Leukoderma Acquisitum Centrifugum (Sutton), Arch. Dermat. & Syph. **7**:611 (May) 1923.

11. Weber, F. P.: A Law Regarding the Distribution of Depigmented Patches of Vitiligo, When They Are Superadded to Mole-Like Nevi, Brit. J. Child. Dis. **21**:202 (July-Sept.) 1924.

also a congenital nevus, the opposite of a pigmented nevus, or is it true vitiligo although limited to a circumscribed area?" We are inclined to answer yes to the first part of the question—that we are dealing with a nevus in the sense of a developmental defect and hope to be able to furnish sufficient evidence to corroborate our belief later on. The fact that in so many of the cases hitherto reported the condition ocurred in a child, even to the extent that Weber considered the condition a disease of childhood, should make one think of the probability of the congenital nature of the disease. Weber used a happy expression in describing the condition—that the white patch forms a halo about the black mole. We suggest naming the disease described by Sutton halo nevus.

Narducci [12] reported two cases, in one of which there were several depigmented patches each containing a pigmented nevus. These he called leukopigmentary nevus, another suggestion for an appropriate name. In the other case there were patches of vitiligo, and in only one of them was there a nevus. He thought that in the second case the peculiar arrangement was accidental, and he called it perinevic vitiligo. The skin in the depigmented portion was apparently normal.

In 1924 von Poor [13] reported a case in which numerous pigmented nevi were surrounded by white areas. There were also pigmented moles without an achromic rim. These were the smallest ones found. He had the impression that the white halo formed only when the mole increased sufficiently in size. The white halo grew in proportion with the increase in size of the pigmented nevus. The patient also observed a gradual increase in the number of lesions. He found islands of pigment in the epithelium of the white area and claimed that the presence of these islands differentiates this disease from vitiligo, in which the depigmentation is complete. His views coincide with those of Stokes, who expressed the belief that the depigmentation is due to a physical or chemical disturbance in tissue balance.

Leszczinsky [14] in his article on Sutton's disease stated that there is a difference in the dopa reaction between this disease and posttraumatic leukoderma. By using the von Groer scale, he found in the normal skin of his patient a value of 16, in the vitiligo-like halos about the nevi a value of 4 and in posttraumatic leukoderma a value of 0. His patient stated that pigmented nevi had been present from birth. There were numerous larger and smaller pigmented nevi which were surrounded by

12. Narducci: Sul neo leucopigmentario et sulla vitiligine perinevica, Arch. ital. di dermat., sif. **1**:271, 1925.

13. von Poor, F.: Ueber Leukoderma centrifugum acquisitum, Dermat. Wchnschr. **80**:401, 1925.

14. Leszczinsky: Ueber Suttonsche Krankheit, Dermat. Wchnschr. **82**:575, 1926.

a white oval or rounded zone. There were also a number of lesions of molluscum fibrosum with a white halo. In one instance the fibroma itself was depigmented. He stated that the size of the white patch was in exact proportion to that of the nevus, being large when surrounding a large nevus and extremely small when in relation with an almost imperceptible pigmented spot. He observed the simultaneous development of the lesion, starting from a barely perceptible speck to the larger central nevus and its halo. This appears to us significant and makes us feel that both are part and parcel of one process. Significant also is the occurrence of the white halo about the fibromas which were present, and as molluscum fibrosum in itself may represent a nevus in the larger sense of the word, we have another variety of the same disease.

Crawford [15] reported the case of a girl who stated that she had had pigmented moles from birth and that the white halos developed recently. This patient also had several patches of vitiligo. Crawford observed an area of hyperpigmentation around one lesion of leukoderma acquisitum.

Krantz [16] reported the case of a patient who had a patch of vitiligo in the center of which there was a hairy pigmented nevus.

Several other cases were reported, but none of them presented any features which might throw light on the subject.

REPORT OF FIVE CASES

Case 1.—Mrs. F. DeS., 36 years old, was a patient in the Morrisania City Hospital, complaining of cardiac disease. When the members of our service were called to see the patient in consultation, there were two white patches, one on the back and the other on the lower part of the abdomen. The lesion on the abdomen was oval, with sharp borders, and measured about 1½ by 2 inches (3.7 by 5 cm.) in diameter. The lesion on the back was somewhat larger. The skin was soft and pliable and, aside from its color, appeared in every way normal. In the exact center of each patch was a light brown raised papule. These structures were soft; the surface was somewhat wrinkled, and to all appearances they were pigmented nevi. The size of each nevus bore a direct relation to the size of the white patch.

Pressure with the diascope over the edge of the white area caused a diminution in the contrast in color between that and the normal skin, but the contrast was not entirely eliminated. Striking the area vigorously with the palm caused a reddening of the normal skin, but the white spot remained unaffected. Application of a mustard plaster over one of the patches for fifteen minutes caused a marked erythema of the surrounding normal skin, but the white patch remained unaffected. There was no disturbance in the sense of pain, but the sense of heat and cold was decidedly impaired in the achromic patch. The tactile sense remained intact.

15. Crawford, S.: Leukoderma Centrifugum Acquisitum, Arch. Dermat. & Syph. **9**:394 (March) 1924.

16. Krantz: Naevus in vitiliginöser Stelle, Zentralbl. f. Haut- u. Geschlechtskr. **16**:872, 1924.

The skin immediately surrounding the white zone showed mild hyperkeratosis, and the granular layer was present but not marked. The stratum Malpighii was normal and consisted of six or seven layers. A moderate amount of melanin was found in the basal cells. The distribution of the pigment was patchy. The chorium was normal and made up of loose bundles of connective tissue, poor in cellular elements. In the papillary layer the fibroblasts were more abundant. No hair follicles or sebaceous glands were encountered. The blood vessels were apparently normal.

At the junction of the normal skin with the white patch the epidermis was still normal, but no pigment was seen in the rete. No chromatophores were

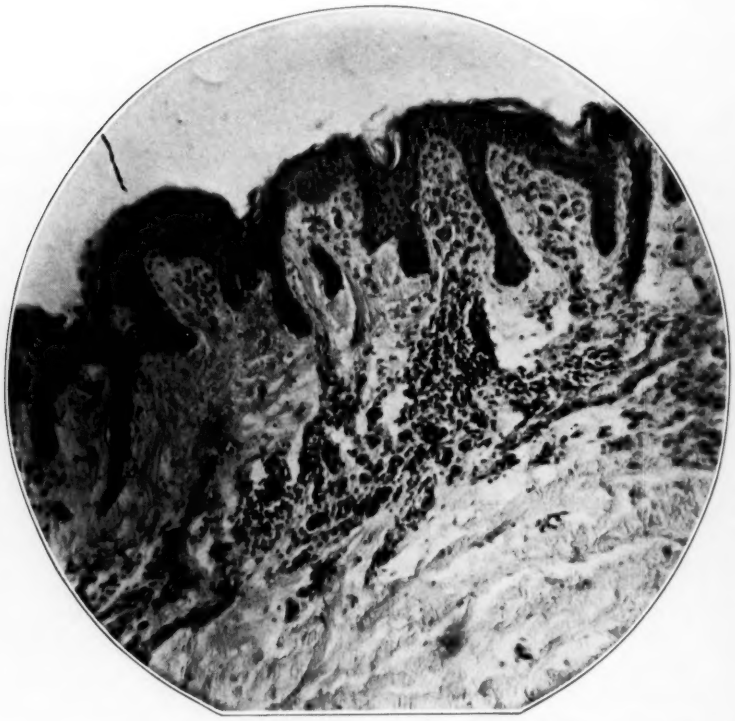

Fig. 1 (case 1).—Photomicrograph of a section from the central pigmented nevus.

noted, but a few scattered free pigment granules were found in the upper layers of the cutis.

In the vitiliginous area, the epidermis was strikingly thin, not more than four or five layers deep and in some places even less. In these locations the papillae were missing and the rete pegs were absent, so that the junction of the cutis and the epidermis was a straight line. The corneal layer was nearly missing and showed some parakeratotic cells. The granular layer was almost absent. In the cutis there was dilatation of the lymphatics and dilatation and engorgement of the capillaries, especially in the subpapillary and upper layers. Some of the engorged capillaries showed perivascular edema, with a minimal amount

of surrounding cellular infiltration, consisting of mononuclear cells. The elastic tissue immediately below the epidermis was fragmented or missing in nearly all areas of the section. It appeared to be diminished in amount in the deeper layers also. Pigment seemed to be entirely lacking in this location.

Near the center of the lesion the rete became more normal in appearance and the papillae and rete pegs became again evident.

In the center of the lesion, the area representing the central pigmented spots, the epithelium was of normal thickness and was thrown into folds. The hyperkeratosis was less marked, but there were a few parakeratotic cells in the section. The granular layer was extremely sparse and for the most part missing.

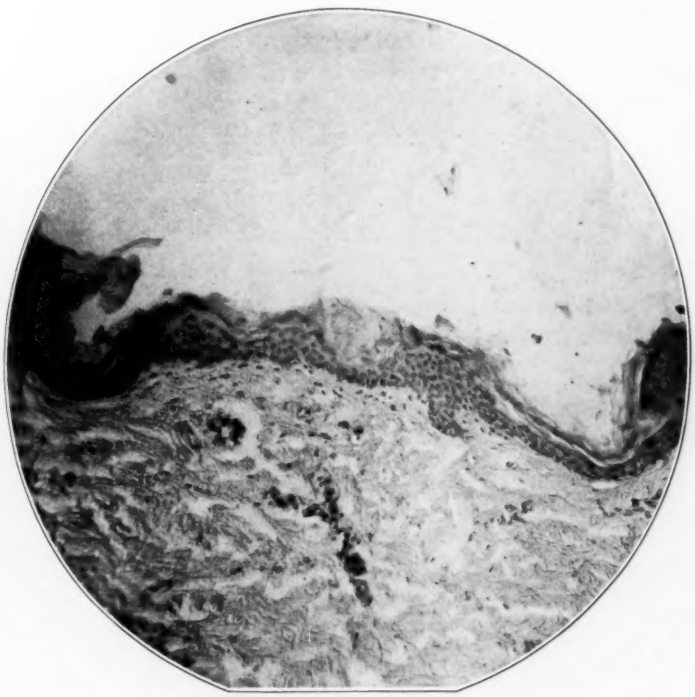

Fig. 2 (case 1).—Photomicrograph of a section from the depigmented halo.

The rete and basal cell layers were normal. There was acanthosis. Some of the interpapillary pegs were extremely long and narrow, and the free end was either spindle-shaped or bulbous. Some of these structures had a constricted neck and gave the impression that they were ready to be snared off. The basal layer contained a large amount of pigment. This was especially true of the swollen ends of the rete pegs. In the subpapillary zone were groups of cells with large, well stained vesicular nuclei and a good amount of protoplasm. There were no fibers between the individual cells, but the groups were separated by septums of connective tissue. Several large multinucleated cells were seen. Some of the cell groups were arranged perpendicularly in the form of long strands occupying the entire length of the papilla and almost reaching the apex, thus presenting a

picture of a typical intracutaneous pigmented nevus. A small number of lymphocytes were present in the corium. Pigment was not abundant in the nevus cells, and only a few islands were densely packed with pigment.

The silver stain revealed the absence of dendritic cells in the epidermis. Several cells which gave the appearance of chromatophores were seen in the cutis, but they were indistinct and could not be differentiated with certainty from the nevus cells.

From the pathologic changes it becomes evident that, at least in this case, the condition is probably not simple leukoderma or even vitiligo and that, except for the pigmentary disturbance, the deviations from the normal structure of the skin which we found in the excised patch are usually foreign to leukoderma or vitiligo. It is remarkable that these changes, which were fairly well defined in the microscopic section, were not so evident clinically. However, if we add to the pathologic observations the lack of response of the blood vessels of the white patch to external irritation as evidenced by the response to striking the area and to the application of a mustard plaster and the diminished sense of heat and cold, the picture becomes definite.

That the lack of response of the blood vessels to irritation may apply also to cutaneous reactions which are due to hematogenic causes is evident from the following case history.

Case 2.—While the patient in case 1 was still under observation, Dr. Jacob Segal came with a youth about 19 to the office of one of us (Dr. Feldman) for consultation about an eruption which was diagnosed as rubella. The eruption covered nearly the entire body; the macules were so numerous that they became confluent, and in places the skin was uniformly red. Among such red areas there was a white patch about 3 by 4 inches (7.5 by 10 cm.) in diameter. Its location was in the lower part of the dorsal region. The outline was not round or oval but somewhat irregular. The borders were sharply demarcated, but they appeared to be scalloped. Occupying the center of this white patch was an elevated brown spot about 0.5 cm. in diameter. This appeared to be an ordinary pigmented nevus. There were no macules or the slightest degree of redness within the limits of the white patch. The contrast between this and the congested skin was striking. There was a difference in temperature between the white patch and the affected surrounding skin. This difference could easily be determined by palpation. Without the presence of the central nevus one would not hesitate in diagnosing this condition as naevus anemicus. As it was, the findings in this case stimulated us to perform the simple experiments which were made on patient 1, and we were surprised with the results.

When the patient returned for reexamination several months later, the eruption was gone, but the achromic patch was still decidedly whiter than the normal skin. A number of enlarged capillaries were present at the border of the patch. This condition has been noted by a number of observers in naevus anemicus.

When the area which included the white patch was struck briskly with the palm, the normal skin became reddened but the color of the achromic patch remained the same. The same condition prevailed after vigorous friction. On pressure with the diascope the normal skin became blanched, but the achromic

patch was still whiter than the normal skin under the diascope. There was diminished sensation for heat and cold. The tactile sense was as keen in the white patch as it was in the normal skin.

Injection of a 1 : 1,000 solution of epinephrine hydrochloride at the margin of the lesion caused blanching of the normal skin. As far as the achromic patch was concerned, it was difficult to say whether there was an increase in whiteness or not, but the portion of the achromic patch which was acted on by the epinephrine appeared to be somewhat lighter than the surrounding blanched skin.

An injection of 0.03 cc. of a 1 : 1,000 solution of histamine hydrochloride was made intradermally into the white patch and also into a normal area about 8 inches (20 cm.) distant as a control. A wheal with pseudopodia formed in each location. The one in the vitiliginous area was about 8 mm. in diameter, while the diameter of the one in the normal skin was about 6 mm. A deep red areola about 4 inches (10 cm.) in diameter formed about the wheal in the control. In the achromic patch the areola formed was much smaller and was very pale pink. In one location the areola included a portion of the normal skin outside the patch. This portion was deep red, not pink. One would judge that the proportion of depth of color between the areola of the achromic patch and that of the normal skin was 1 : 5. The redness within the white area disappeared within thirty-five minutes, while that of the control area was reduced by less than half in the same span of time. The wheal persisted longer in the achromic area than in the control area.

In order to verify these findings and for the purpose of comparison, we repeated the experiment on a patient with ordinary vitiligo. There was a difference in the depth of color between the areola in the area of vitiligo and that in the normal skin, but in spite of the fact that the surrounding skin was hyperpigmented, the difference was comparatively slight and could be easily accounted for by the difference in the original color.

Another and even stronger verification of our point of view that in the two reported instances of so-called Sutton's disease the patients had, in addition to the pigmentary disturbance, a disturbance in the circulatory mechanism, presumably due to improper innervation was furnished by the following case.

Case 3.—E. K., an 11 year old schoolgirl, came to the Morrisania clinic on Dec. 16, 1935, with an eruption of discrete red papules over the arms and trunk. The papules were arranged in lines, circles and semicircles, indicating a follicular distribution. There were two large patches, each about 4 by 5 inches (1.10 by 12.5 cm.) in diameter, on the left side of the trunk. Smaller patches were present, two on the right side and two on the back. The mother stated that the child had the condition since early babyhood but that she had not noticed it at birth. The papules appeared in the vitiliginous areas approximately in the same number as on the normally pigmented skin. The girl was a brunet, with a good amount of pigment in the skin, but the borders of the white patches were no more pigmented than the rest of the skin. If one is to stress the hyperpigmentation at the border as an essential diagnostic symptom of leukoderma or vitiligo, this patient's condition does not fall into that category. Is hyperpigmentation at the border of a depigmented patch overestimated as a symptom of these two conditions, or is the condition in this case something else, for instance the albinism partialis described by some authors?

When the eruption had cleared up, the reactions were tested in the same manner as those in the preceding cases, and no deviation from the normal function of the skin was found in the patch. Pressure with the diascope did not obliterate the difference in color between the white patch and the normal skin. An injection of histamine hydrochloride at the border of the patch caused the formation of a

wheal and a bright red areola around it. The areola was situated partly on the normal skin and partly on the patch. The color was nearly uniform in the entire areola, and hardly a perceptible difference could be seen, in spite of the fact that the girl had a fairly dark skin.

From the study of the first two cases cited, one can readily see that the achromic area in so-called Sutton's disease is not necessarily a simple leukoderma but at times may show structural and functional changes which are usually not seen in leukoderma or vitiligo. In these two cases the functional changes, except for the pigmentary disturbance, were identical with those seen in naevus anemicus. Unfortunately, it was not possible to obtain permission for a biopsy in the second case, and for that reason it was not possible to ascertain the amount of depigmentation or apigmentation, if any. It was possible, however, to compare the clinical features with those in our first case or, for that matter, with any condition which might throw some light on the subject.

Soon the opportunity offered itself to us to compare the condition in this case with that in a case of frank naevus anemicus. This furnished us with what we thought to be valuable information.

Case 4.—R. R., a housewife, was admitted to the Morrisania City Hospital on Nov. 10, 1935, suffering from an acute gynecological condition. She received several injections of codeine sulphate and stated that she had taken acetylsalicylic acid before admission to the hospital. After she had stayed a few days in that institution, there developed a rubeola-like eruption on the front and back of the trunk, abdomen and lumbar region. On the back the eruption became confluent, to form a generalized scarlatiniform erythema, extending from the neck to the buttocks. In the sacro-iliac region there was a patch about 3½ by 4½ inches (8.7 by 11.2 cm.) in diameter. This patch was white and, as far as appearance was concerned, was unaffected by the eruption. The borders of the patch were sharply demarcated from the surrounding erythematous skin, and at the margin there was a comparatively large number of small white patches, ranging in size from that of a pinhead to that of a pea or larger.

The patient reported at the clinic on Dec. 2, 1935. At that time the eruption had disappeared, but the white patches were as clearly visible as they had been when it was present, although the contrast was not as marked. Pressure with the diascope made the patch invisible on account of the blanching of the normal skin. When the region of the white patches was struck with the palm, the normal skin became reddened, while the white area remained unaffected.

Injection of a 1 : 1,000 solution of epinephrine hydrochloride intradermally at the border of the white patch caused a blanching of the normal skin. The action of the epinephrine extended to a portion of the white patch, and this, together with the blanched normal skin, was considerably lighter than the rest of the white patch, which was not acted on by the epinephrine, indicating that, even in this location, a certain amount of color was due to circulating blood.

Tests of the reaction to heat and cold made in the same manner as those in the other cases showed a marked diminution of that sense in the white patch as compared with the normal skin. There was no difference in the sense of touch. Vigorous friction of the area with a pad soaked in turpentine caused reddening of the normal skin, while the white patch remained unaffected.

Injection of 0.03 cc. of a 1:1,000 solution of histamine hydrochloride intradermally into the center of the white patch caused the formation of a wheal within a few seconds. This wheal gradually increased in size until when fully developed it measured about 1 cm. in diameter. Surrounding this wheal a faint flush appeared immediately after the injection. The color was not uniform but gave the impression that certain capillaries were first to dilate. Soon, however, the color deepened to a light pink and formed a uniformly colored areola about the wheal. The same quantity of histamine was injected into the normal skin at the angle of the scapula. The wheal formed was somewhat smaller than the one in the white patch, but the surrounding areola which was formed immediately after the injection was much larger, about 2½ inches (6.2 cm.) in diameter, and deep red.

It was difficult to explain why the wheal formed after an intradermal injection of histamine hydrochloride in the white patch in naevus anemicus and in one of the cases of Sutton's disease described was larger than the one formed after an injection of the same quantity of histamine into the normal skin, whereas in the case of the areola the process was reversed, and the areola in the achromic patch was insignificant. Is it perhaps that the diffusion of the drug into the neighboring vessels and tissues was diminished in the affected region, the drug remaining confined mostly to the region injected and exerting a greater local influence on the vessels?

The only points of difference between naevus anemicus and the condition in the first two cases was that it was possible in the case of naevus anemicus completely to wipe out the difference in color between the affected area and the normal skin by simple pressure with the diascope or by the injection of epinephrine hydrochloride at the border of the patch. It was not possible to obtain the same effect in the other two cases, and it was undoubtedly due to the diminution or absence of pigment.

CASE 5.—A patient from the Mount Sinai clinic, 22 years of age, born in Puerto Rico, stated that she had observed the condition of her skin about two years before admission and that the lesions since that time had increased in size and in number. On examination there were noted about a dozen oval or rounded sharply defined areas, which were white and apparently devoid of pigment. In the center of each white area was an elevated light brown spot which resembled an ordinary pigmented nevus. The larger lesions were from 1 to 1½ inches (2.5 to 3.7 cm.) in diameter, the smallest not larger than a pea. They were scattered over the trunk and extremities. One lesion was situated on the vulva. A number of pigmented nevi without white halos occurred among the others. It was not possible to elicit from the history given by the patient whether the vitiliginous patch or the hyperpigmented central spot was the first to appear. To us it seemed that in one of the patches, at least, the white area was primary and the pigmented mole made its appearance in a preformed white patch. This was deduced from the fact that in the lesion referred to the central elevated spot was so minute when first observed that it was almost imperceptible and since then it had enlarged to the size of a large pinhead. A short time before her admission a new white patch without a central spot made its appearance.

The biopsy, made by Dr. Samuel Peck, showed the presence of a typical nevus with typical nevus cells in one part of the section. There were practically no pigment cells in the central nevus. As a matter of fact, only one or two cells which contained melanin could be seen. This was demonstrated with the silver stain only. The rest of the section showed a rather thin epidermis with no other pathologic changes except that no pigment was to be seen in any of the basal cells or the overlying rete.

Application of a freshly prepared mustard paste over the region of one of the white patches caused a reddening of both the normal skin and the vitiliginous patch.

Injection of 0.03 cc. of histamine hydrochloride into the white patch caused the formation of a wheal with a red areola. Injection of the same amount intradermally into the normal skin also caused a wheal and an areola which was deeper in color than the one in the white patch, but the difference in shade could be explained by the absence or presence of pigment.

Pressure with the diascope did not eliminate the difference in color between the white patch and the normal skin.

We availed ourselves of the offer of Dr. I. Rosen to include this case from his service because it represented the reverse side of the medal—namely, no changes were present except the depigmentation. Even this is not entirely correct, as the section revealed a considerably thinner epidermis than is usual for the location from which the section was made.

In perusing the very meager literature on the subject one finds that the pathologic changes in the cases so far described are extremely variable. There seems to be a gradation from a nearly normal condition of the skin in the white patch to pathologic changes which are akin to real atrophy. Thus, depigmentation was incomplete in the case reported by von Poor, in which islands of pigment were found in the epithelium of the white patch. Most writers, however, have mentioned a normal but depigmented skin. There were other cases in which, excepting the achromia, there was the barest evidence of a pathologic condition, as in our case 5, in which the biopsy section revealed an epidermis which was thinner than was usual for the location from which the section was taken. Almkvist, on the other hand, did not mention any microscopic changes in the white patch in his case but stated that, in addition to the pigmented nevus in the center, the condition presented all the features of naevus anemicus. In our case, in addition to the clinical features of depigmentation and naevus anemicus, there were the pathologic changes of early atrophy, even including the degeneration of the elastic tissue which is so characteristic of atrophy. While this case has no parallel in the literature, it is backed up by the similarity of the clinical features to those of our second case and the case of Almkvist. We feel that had the pathologic changes in more of the cases reported been carefully studied, the condition would not appear to be unique. On

the other hand, Lévy-Franckel, Guilhaume and Juster [17] found edema and diminution, constriction and disappearance of capillaries in a patch of what appeared to be clinically ordinary vitiligo. Similarly, in speaking of vitiligo, Gans [18] said that there are atrophic and inflammatory changes in the vitiliginous area along with nerve changes which are difficult to interpret.

Another characteristic of leukoderma acquisitum should serve to separate the condition in these cases from the general class of leukoderma and vitiligo. Chromatophores are supposed to be abundantly present at the margin of the lesion in leukoderma and in vitiligo, where they exert a phagocytic action on the melanin. In our cases, in those of Stokes and in others in which the pathologic changes were studied, chromatophores were conspicuous by their absence; hence there was no phagocytic action to explain the depigmentation.

So much for the pathologic picture. The clinical picture is as varied as the pathologic findings. Cases have been reported in which there were lesions consisting of a central mole with a surrounding white halo. In others these lesions were present in addition to achromic patches without central nevi, while in still others the patient had typical lesions of leukoderma acquisitum as well as achromic patches without centrally located pigmented spots and numerous pigmented nevi without white halos.

The central nevus varied from a small, insignificant and barely pigmented spot to a large, deeply pigmented, verrucous and hairy nevus. In one case lesions of molluscum fibrosum with white halos were present side by side with the typical lesion.

The regularity of the shape of the white patch, its almost constant round or oval configuration, with sharp borders, and its proportionate size to that of the central nevus indicate a rather more than casual occurrence of these lesions, and, to our way of thinking, there is no question that these lesions constitute a clinical entity. The existing uncertainty refers to their interpretation only. Those who consider the condition a primary and unusual form of vitiligo, the central spot being the reversal of the hyperpigmented border, will find solace in the fact that some lesions start as an achromic patch, the pigmented center developing later, while those who correctly consider the central spot a real nevus, the white portion being vitiligo which is caused by the presence of the nevus, will find apparent corroboration in the cases in which the lesion supposedly starts with a nevus and the white halo develops about it. On the other hand, if we take into account the findings of Leszczinsky, who stated that he saw the two lesions develop simultaneously, and

17. Lévy-Franckel, Guilhaume and Juster: Cutaneous Circulation in Alopecia Areata and Vitiligo, Presse méd. **33**:1050, 1925.

18. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925.

if we add to it the clinical and laboratory findings, which show a variation from a simple achromia to that of depigmentation plus the features of naevus anemicus, we cannot help being convinced that we are dealing with a nevus consisting of two component parts, one a true intracutaneous nevus which may or may not be pigmented and the other a nevus in the broader sense of cutaneous malformation. We assume that the central nevus may at times not be pigmented because of the reported findings of molluscum fibrosum, which may in reality be a true nevus, and because of the surprisingly small amount of pigment noted in the nevus cells in nearly all biopsy specimens.

Stokes' conception of the causation of the achromia appears to be the most plausible one, in spite of the fact that there were undoubted cases in which the vitiligo preceded the pigmented nevus at least clinically. We believe, however, that the two parts of the nevus originate simultaneously but that in some cases the pigmented nevus is so small that it is invisible on the surface, or the nevus may lack color and for the time be overlooked. It would be interesting to make serial sections of some of the achromic patches which occur in Sutton's disease and are clinically without a central nevus. This we hope to do when the opportunity offers itself. Our views coincide with those of Stokes only so far as we believe that the white lesion is caused by a physical or chemical disturbance in equilibrium of the tissues about the nevus. We cannot agree with him that the central nevus is the cause of that disturbance, but we believe that both the central nevus and the achromia are caused by a loss of tissue equilibrium which is congenital and is in accord with the theory of Connheim.

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PURPURA ANNULARIS TELANGIECTODES

REPORT OF A CASE

STUART C. WAY, M.D.
SAN FRANCISCO

Majocchi [1] in 1896, after having observed three cases of a similar condition, described an unusual disease of the skin, characterized by the presence of minute telangiectatic puncta, which form various-sized annular lesions that disappear in the course of time, with or without atrophy.

In 1915 MacKee [2] completely reviewed the literature and at the same time reported the thirty-ninth case.

Among the more recent authors to describe this interesting disease are: Copelli [3] and Angelini,[4] 1915; Semon,[5] 1920; Balzer,[6] 1926; Majocchi,[7] 1928; Marchisio [8] and Scholtz,[9] 1929; Gottron,[10] Cavallucci,[11] Curle and Smith [12] and Way,[13] 1930; Ciarrocchi [14] and Selissky,[15] 1931; Ferrabouc, Massia and Friess,[16] 1932; Nordin [17] and Levin and Tolmach,[18] 1933.

From the Department of Dermatology, Mary's Help Hospital.

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17. Nordin, G.: Acta dermat.-venereol. **14**:369 (Nov.) 1933.
18. Levin, O., and Tolmach, J. A.: Purpura Annularis Telangiectodes, Arch. Dermat. & Syph. **28**:384 (Sept.) 1933.

REPORT OF CASE

Mrs. W. B., aged 32, a housewife and resident of Santa Rosa, Calif., was born in California of Danish-American parents. She had always lived on a farm and been accustomed to heavy work. Her father died of heart disease at the age of 75. Her mother died of cerebral hemorrhage. An infection due to Trichina caused the death of one sister. There was a definite history of tuberculosis on the father's side of the family, several members having been affected.

The patient had the usual diseases of childhood, including varicella, whooping cough and scarlet fever. Menstruation began at the age of 11. A complete hysterectomy was performed on the patient at the age of 26. There were two children, a boy aged 10 and a girl aged 11.

In the fall of 1932 the patient had a severe infection of the antrum, which subsided as soon as drainage was established. Her physician stated that a culture of the material from the antrum was not made. At the time of this infection a dermatitis developed about the ankles, which resembled the present cutaneous involvement. Three or four months elapsed before it disappeared.

During the fall of 1933 there was a recurrence of the sinus infection and of the dermatitis about the ankles. Apparent recovery from both took place as before, in the same length of time.

On Dec. 21, 1934, the patient called at the office, complaining of a dermatitis limited to the lower extremities, which had itched intensely since its onset, six weeks before. The cutaneous manifestations, as in previous years, followed a severe infection of the sinus.

Physical Examination.—On examination the patient appeared to be of normal intelligence, free from all neurotic tendencies. Her height was 5 feet, 2 inches and her weight 200 pounds (90.6 Kg.). The infection involving the antrum had temporarily cleared up. A few varicella scars were present about the face, but scars suggestive of syphilis, tuberculosis, etc., were lacking. Minute superficial varices, commonly seen about the legs, were also absent, and except for the eruption and considerable dermographia nothing unusual could be detected.

Description of the Eruption.—The eruption was located on the anterior and lateral surfaces of the legs, between the ankles and the knees and also about the ankles, where it was most profuse. The mucous membranes and other parts of the body were not involved.

The earliest lesions, of macular type, varied in size from that of a pinpoint to that of a pinhead, were bright red and occurred independently of hair follicles.

Diascopic pressure caused a paling of the lesions but no alteration in the color of the hemorrhagic dots. The lesions enlarged by peripheral extension to a diameter of from 3 to 4 cm. and cleared centrally but left a brownish pigment, while the reddened borders contained innumerable telangiectatic puncta. The occasional joining of annular lesions produced varied configurations. Furfuraceous scaling was also present. The sites of the older lesions were indicated by brown pigmentation of various shades, depending on the age of the lesion, but atrophy, noted by some observers, could not be detected. Various-sized pale red elevated papules, clinically characteristic of urticaria, were present on the anteroposterior and lateral surfaces of the knees. These lesions lacked the hemorrhagic puncta, telangiectasia and pigment common to purpura annularis telangiectodes.

Laboratory Examination.—The Kolmer, Kahn and Pirquet tests gave negative results. The blood count showed leukocytes 18,760, erythrocytes 4,630,000 and

platelets 288,000. The coagulation time was three minutes and forty-two seconds. The hemoglobin content was 80 per cent (Sahli), and the color index, 0.97. The differential count was as follows: polymorphonuclears 53 per cent, lymphocytes 27 per cent, monocytes 16 per cent, eosinophils 3 per cent, basophils 1 per cent, segmented polymorphonuclears 44 per cent and banded polymorphonuclears 9 per cent.

The urinalysis showed specific gravity 1.018, no albumin or sugar and an acid reaction. A centrifugated specimen showed many oxalate crystals and numerous epithelial cells, about 6 per high power field. There were 4 pus cells per high power field.

Biopsy.—A section of skin representing the hemorrhagic pigmentary stage of the disease was removed from the outer surface of the left ankle. The tissue was fixed in alcohol, embedded in paraffin, cut in serial sections and stained as follows: with hematoxylin and eosin, hematoxylin and orange "G," polychrome methylene blue, Gram's iodine, and orcein; by Weigerts', Giemsa's, Pappenheim's and Ziehl-

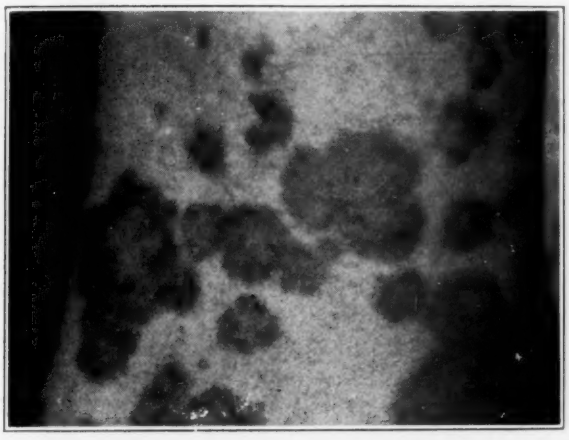

Fig. 1.—Area from the outer aspect of the left ankle. One of these isolated lesions was removed for microscopic study.

Neelsen's methods and according to Perles' test for prussian blue reaction for hemosiderin.

Microscopic Study.—Under low power one noticed an increase in the number of small capillaries; they were dilated, and cellular infiltration surrounded them and the coil glands. This vascular dilatation occurred throughout the dermis and the subcutaneous tissue.

Epidermis: The stratum corneum was moderately thickened, and perifollicular parakeratosis could be noted in practically all of the sections. This parakeratosis caused the occlusion of many of the sweat gland ducts, and their consequent dilatation in some instances involved the body of the gland itself. Several sections showed enormously dilated ducts, occurring within the epidermis, which were completely filled with various products of excretion together with a few leukocytes. Intercellular edema and epidermal necrosis explained in part the interference with the normal evolution of the epidermal cells and accounted for the thickening of the

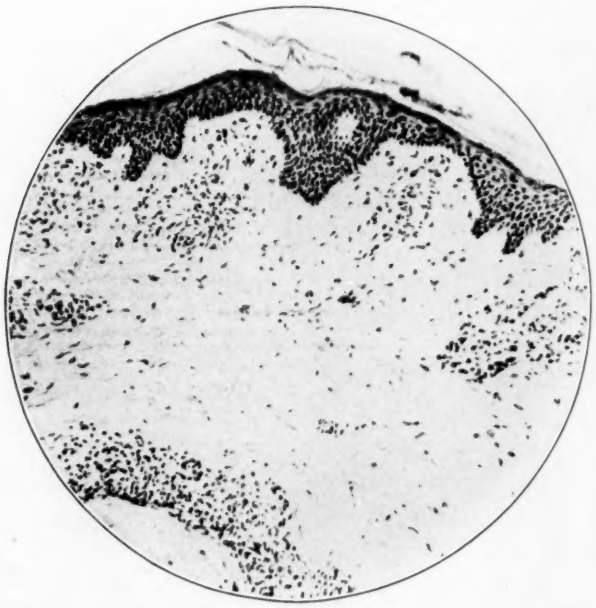

Fig. 2.—The vessels throughout are dilated and surrounded by infiltrating cells. Hematoxylin-eosin stain; × 120.

Fig. 3.—Dilated sudoriparous duct within the epidermis, containing leukocytes and other products of excretion. Weigert's hematoxylin stain; × 300.

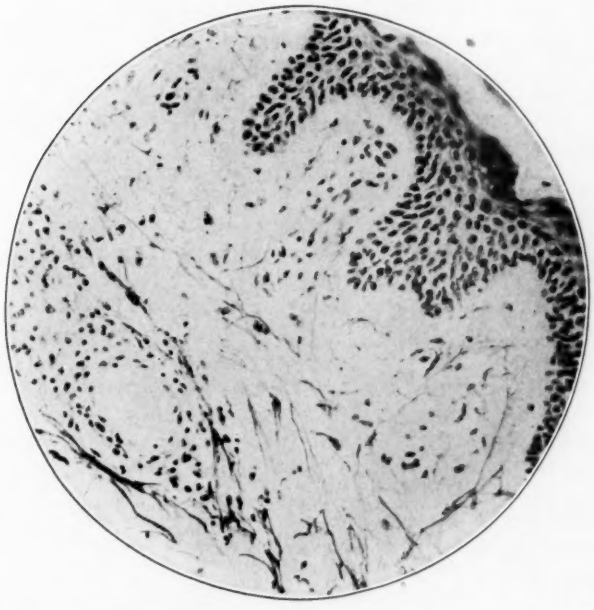

Fig. 4.—Papillary edema, vascular dilatation and an enormously distended sudoriparous duct. Weigert's hemtoxylin stain; × 200.

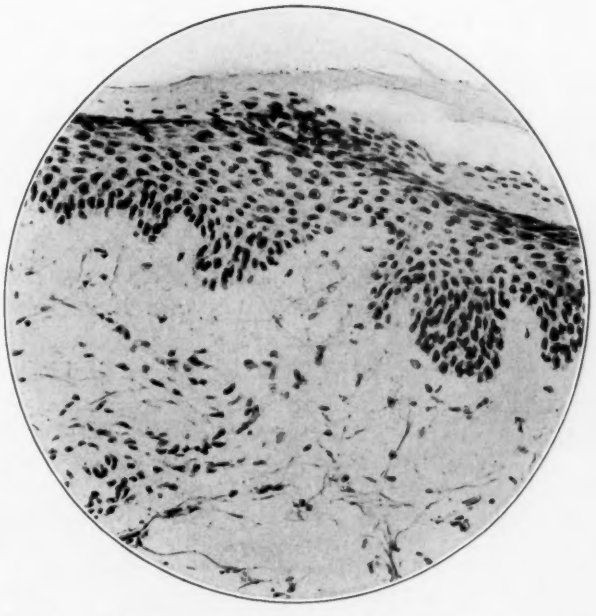

Fig. 5.—Parakeratosis and an epidermal micro-abscess. Weigert's hematoxylin stain; × 300.

corneum and the exfoliation which Highman [19] has mentioned. Nonhematogenous pigment occurred extracellularly and intracellularly near and within the basal layer.

Dermis: The upper layers of the dermis, especially the papillary layer, were edematous. There was a distinct increase in the number of the smaller capillaries, and although they were widely dilated, hemorrhage as a result of the rupture of a capillary or diapedesis could be neither observed nor demonstrated by Perles' test.

Throughout the subpapillary layer many of the vessels presented alterations in their walls. In some the endothelium had proliferated and become swollen and caused almost a complete occlusion of the lumen. Tiny aneurysmal sacculations in longitudinal sections were occasionally seen in the walls of the vessels, when the wall was thin and ballooned out. Near by were extravasations of serum. Although this vascular dilatation persisted throughout the deeper part of the dermis and also within the subcutaneous tissue, few of the vessels were filled with blood.

The infiltrating cells, consisting of lymphocytes, endothelial cells and eosinophils, were noticeably dense about the subpapillary vessels and the sudoriparous glands and ducts.

The elastic fibers were apparently normal, except in the infiltrated areas, where they were either swollen or completely absent.

The degree of degenerative change that the sweat glands showed seemed to depend on the density of the infiltrating cells, but in no instance had the glands completely disappeared. A few of their ducts were widely dilated.

The hair follicles and sebaceous glands were little affected. Sections stained by Ziehl-Neelsen's method gave negative results for acid-fast bacilli when examined by Hoffmann's [20] dark-field method.

COMMENT

The following factors in this case coincided with Majocchi's original description of the condition: (1) the appearance of the eruption, except for the follicular occurrence; (2) the slow, progressive development by peripheral extension and the formation of annular lesions; (3) the symmetrical distribution of the lesions and (4) the location of the eruption, that is, the fact that it was present only on the extremities.

In the following respects the case under consideration differed from that observed by Majocchi: (1) in the intense pruritis (all lesions); (2) in the tendency to recur annually; (3) in the coexistence of the infection and papular urticaria; (4) in the absence of terminal atrophy, and (5) in the fact that the condition followed a definite sinus infection.

Although several authors, including Majocchi,[1] Ossola [21] and Verrotti,[22] have commented on the pruritus which preceded the eruption,

19. Highman, W. J.: Dermatology, New York, The Macmillan Company, 1921, p. 86.

20. Hoffmann: Die Bedeutung der Leuchtbildmethode zur Darstellung von Mikroorganismen, Dermat. Ztschr. **33**:6, 1921.

21. Ossola: Gior. ital. d. mal. ven. **46**:250, 1911.

22. Verrotti, G.: Gior. internaz. d. sc. med. **33**:167, 1911.

I do not believe that in their cases the condition was complicated by coexisting urticaria. Apparently in this case the two diseases occurred independently of each other, for in July 1935 typical papular urticaria again appeared on the patient's lower extremities, but there was no evidence of purpura and the eruption disappeared within a few days, without pigment formation.

The pathologic picture in this case was in close agreement with that in the cases already reported, but, as in MacKee's [23] description, the amount of hemorrhage noted microscopically was almost negligible, although clinically considerable appeared to exist. As has been stated, this clinical picture may be due to the fact that thrombosed or angiectatic superficial capillary loops are dark red, fail to pale on pressure and may simulate hemorrhagic puncta.

A more definite relation to infection seems to be established in the instance under consideration than in the cases previously reported. The infection of the antrum from which the patient suffered at the time of examination seemed to be the explanation for the leukocyte count of 18,760. Recurrence and remission, such as those described in this paper, have been called a part of the clinical picture of purpura annularis telangiectodes.

SUMMARY

A case of purpura annularis telangiectodes occurring simultaneously with urticaria is reported.

Acid-fast bacilli and Russell fuchsin bodies could not be found.

The microscopic changes suggested that the disease was due to a toxin.

The theory of toxic origin seems to be substantiated by the fact that the cutaneous manifestations for three successive years were preceded by a severe sinus infection.

23. MacKee, G. M.: J. Cutan. Dis. **33**:187, 1915.

ETIOLOGY, PATHOLOGY AND TREATMENT OF LEUKOPLAKIA BUCCALIS

WITH A REPORT OF THREE HUNDRED SIXTEEN CASES

FRANCIS P. McCARTHY, M.D.
BOSTON

Leukoplakia buccalis, leukokeratosis or smoker's patch is one of the most common lesions that one encounters in an examination of the oral cavity. A voluminous literature has been written on the subject over many years, and yet several facts about the condition need to be elucidated. It is interesting to note how the authorities differ regarding the relation of syphilitic infection to the development of leukoplakia, and a free discussion by various observers leads invariably to a considerable difference of opinion as to whether syphilis is the most important causal factor.

For the past several years I have classified the cases of this condition in relation to the etiology and studied the histologic changes in the various stages of development of the lesion.

This study of leukoplakia was carried on primarily at the clinic in oral medicine at Tufts Dental School and was extended to include a group of cases observed in the department of dermatology and syphilology of the Boston City Hospital and in private practice. The cases have been studied with particular reference to the incidence of syphilitic infection and to the use of tobacco in its various forms.

GRADES OF LEUKOPLAKIA

In order to indicate properly the types of leukoplakia, I have graded its stages according to the clinical and histologic picture.

Grade 1.—This type is characterized by the initial reaction of the mucous membrane to irritation, indicated by a red, granular, sharply defined, slightly sensitive area, which remains in this stage a short time and later becomes slightly whitish gray. The microscopic picture of the lesion shows a purely inflammatory reaction of the corium, without definite epithelial proliferation.

Grade 2.—In this stage a definite lesion occurs; it is characterized by bluish-white patches or plaques, without palpable induration but sharply outlined from the normal mucosa. The lesion is quadrangular

From the Department of Dermatology and Syphilology, the Boston City Hospital, and the Department of Oral Medicine, Tufts College Dental School.

or irregularly polygonal, and the plaques appear to be pasted on the mucous membrane. Microscopically there is a definite hyperkeratotic and acanthotic change, with a slightly cellular reaction in the corium.

Grade 3.—This grade of leukoplakia is definite and is easily recognized at a glance, even by a layman. It presents a milk-white, pearly or silvery indurated plaque, which may be localized or may cover a large area. The lesion may tend to wrinkle, especially if it involves the buccal mucosa of the cheeks. Microscopically the classic picture of

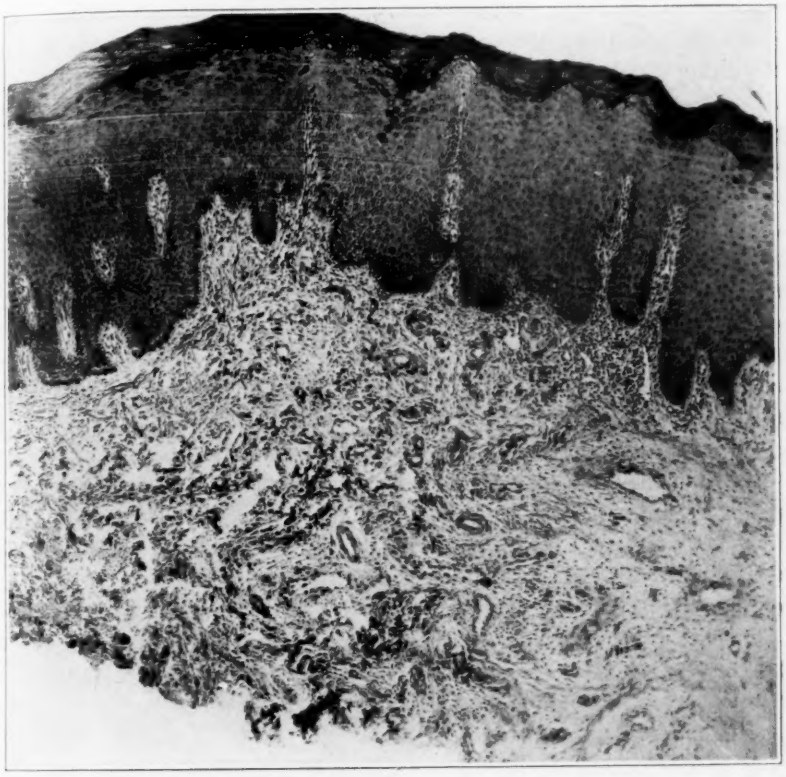

Fig. 1.—Photomicrograph of a lesion from a smoker's palate (fig. 2), showing grade 3 leukoplakia.

marked hyperkeratosis with acanthosis and cellular reaction of the corium is seen.

Grade 4.—This stage, clinically, is observed as a still more pronounced keratotic lesion, indurated and leathery and beginning to show evidence of malignancy, which is recognized by early erosion, by fissuring of the plaque or by the tendency to warty proliferation of the surface. This grade should be treated as an incipient malignant neoplasm.

CLASSIFICATION OF LEUKOPLAKIA ON THE BASIS OF ETIOLOGY

To simplify the classification of the types of leukoplakia from an etiologic standpoint, I have grouped the cases as follows: those in which the condition was due to (1) faulty occlusion, (2) chronic irritation, (3) use of tobacco and (4) syphilis.

Group 1: Faulty Occlusion.—This group was the largest in my collection of cases. On examination of the oral cavity, localized areas of leukoplakia due to faulty occlusion, caused by either natural teeth or artificial partial or full dentures, may be observed in an appreciably large number of persons, especially in those beyond middle life, in whom the irritation has continued over many years. However, it is interesting that in this large group the additional factor of use of tobacco plays an important rôle. Since its use is so general and since it acts as an associated irritant in the cases of leukoplakia due to faulty occlusion, the two factors frequently have to be considered together. Often there is malocclusion which has affected the patient from childhood and has never been properly corrected; the contact irritation of the delicate mucous membrane is an important factor in the production of leukoplakia. This type is more common in the buccal mucosa of both cheeks and is usually a bilateral process, as the occlusal factor is symmetrical. An important type of occlusal disturbance is related to the previous loss of one or more teeth and the use of the gingival margin as a biting surface, so that considerable irritation is brought to bear on the edentulous gingival margin. This condition is particularly common in the region of the third molar when the tooth has failed to erupt or has been removed. It is interesting that in younger persons it is not uncommon to find a tendency for the teeth in apposition to the edentulous gingival crest to protrude from their sockets, to compensate for the lack of dental articulation. A careful search of the oral cavities of persons with dental occlusal defects, especially of those beyond middle life, reveals an extraordinarily high percentage of localized leukoplakic lesions. Most of them, however, are relatively mild and require no treatment, and the introduction of proper bridgework to fill in the dental gaps or the grinding of the occlusal edges of sharp teeth is usually effective in controlling the condition. There is a type of malignant process which begins in the mucous membrane of the gingiva and extends to the jaw by continuity: A focal leukoplakic lesion initiates the epithelial neoplasm, but as carcinoma of the jaw does not arise primarily in bone it is reasonable to assume that the so-called primary carcinoma of the maxilla arises in a leukoplakic lesion of the gingival or adjacent mucosa. In a series of male patients taken at random, who were definitely nonsyphilitic, faulty occlusion was the most common single cause. In women the condition, in the few cases that I have noted, was due to faulty occlusion or to chronic irritation in the oral cavity.

Leukoplakia of the tongue in women is invariably associated with atrophic glossitis due to primary or secondary anemia. In general one may say that the frequency of the condition increases greatly in persons over 40 years of age, especially in those who use tobacco to excess.

Group 2: Chronic Irritation.—In this group are included the cases of focal irritations of the mouth other than those in which the condition is due to the use of tobacco, which I have grouped by themselves. Among the causes of local irritation, other than faulty occlusion, are carious teeth, oral electric currents, sharp edges of crowns and bridges, lingual bars and other dental appliances; habitual biting of the cheeks and lips and hot and spicy foods, the latter significant especially in cases of leukoplakia involving the tongue. I have also included in this group the case of the man who chews tobacco and who usually carries the cud in contact with the buccal mucosa of the cheek. A factor that is important in all cases of leukoplakia, but is especially so in this group, is chronic periodontal infection, with associated lack of dental hygiene. I am convinced that the edentulous mouth, with artificial dentures that fit properly or without them, tends to remain free from leukoplakia. The betel nut quid is a common cause of leukoplakia and of malignant growths of the oral cavity. It is made up of tobacco, betel nut and black catechu. The chewing of this quid liberates various pigments, gallic and tannic acid, oils and bitter substances. The incidence of leukoplakia and of malignant conditions from this type of irritation is about equally divided between the sexes.

Recently there has been considerable literature on the presence of electrolytic currents in the oral cavity.[1] I do not believe that this factor is important in causing focal irritation with resulting secondary leukoplakia.

An improperly vulcanized plate may be a source of chemical irritation, with the secondary development of leukoplakia.

Group 3: Tobacco.—The use of tobacco is generally recognized as the most important factor in the production of leukoplakia and the most frequent cause.[2] To be sure, the irritation due to tobacco is superimposed on other types of irritation, but even by itself it is generally considered to be the outstanding irritative agent in the production of the condition. It is generally accepted that the products of combustion and heat are the underlying sources of irritation to the mucous membrane. Various observers have indicated that the last few centimeters of a cigaret contains a concentration of irritating substances which are

1. Lain, E. S.: Chemical and Electrolytic Lesions of the Mouth Caused by Artificial Dentures, Arch. Dermat. & Syph. **25**:21 (Jan.) 1932.

2. Hollander, L.; Permar, H. H., and Shonfield, L.: Leukoplakia of the Oral Mucosa, J. Am. Dent. A. **20**:41, 1933.

highly injurious to the mucous membrane. From my studies I am convinced that the use of the pipe is by far the most irritating form of smoking. It is difficult to say which is the greater offender in causing leukoplakia, the cigaret or the cigar. As heat is undoubtedly an important factor, I assume that the cigar, especially if it is smoked to the extreme end, generates more heat than the cigaret and therefore, other conditions being equal, would produce more irritation. The tar and nicotine content and the many other injurious irritants in tobacco combine to produce local irritation.

The method of smoking seems to play an important rôle in the localization of leukoplakia. One-sided smokers tend to produce a unilateral involvement, especially of the tongue. Many smokers tend to inhale

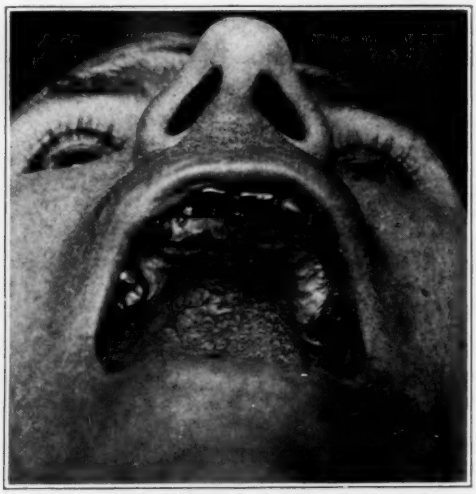

Fig. 2.—A smoker's palate, with grade 3 leukoplakia.

the smoke into the oral cavity in the form of a funnel, and when it is brought into frequent contact with the mucous membrane in the region of the palate, localized plaques of leukoplakia are produced. Probably the most common location for leukoplakia, even more common than the lips, is the buccal mucosa at the angles of the mouth. This fact suggests that the exhalation of smoke through the corners of the mouth is an important source of irritation.[3] The use of the smooth amber mouth piece, in contrast with the old clay pipe, is unquestionably significant in lessening heat as a source of irritation to the lip and tongue. The person who tends to keep the tongue in contact with the end of the cigaret or cigar often has involvement of the tip and anterior margin

3. Landouzy, L.: Leucoplasies jugales et commissurales, Presse méd. **16**:409, 1908.

of the tongue. It is rare to find leukoplakia of the dorsum of the tongue in a nonsmoker; even the patient with a preexisting syphilitic glossitis does not have leukokeratosis of the atrophic mucous membrane unless he is addicted to the use of tobacco. Among the products found in tar and cigaret smoke are nicotine, phenolic bodies, pyridine bases and ammonia. The last ½ inch (1.3 cm.) of a cigaret shows a definite accumulation of irritating substances, particularly of tar and other products of incomplete combustion. Rapid smoking produces a rapid rise in temperature within the oral cavity, and smoking to the extreme end definitely increases local heat. There is no question that heat and the irritation from the products of combustion are the most important causes of the reaction of the tissues that culminates in leukoplakia.

Fig. 3.—A lesion occurring on the tongue of a right-sided, nonsyphilitic smoker; grade 3 leukoplakia.

Group 4: Syphilis.—There is a wide divergence of opinion even today as to the relation of syphilis to leukoplakia. The confusion is undoubtedly due in part to the observations of the older writers, who invariably connected most cases of leukoplakia with syphilis.

After studying 316 cases of leukoplakia, I am convinced that in a high percentage of cases extensive involvement of the tongue is definitely related to syphilis but that there is no evidence to indicate a relation between the greater number of instances of leukoplakia observed elsewhere in the oral cavity and syphilitic infection. The predisposing factor in leukoplakia linguae is atrophic glossitis of syphilitic origin, occurring in untreated or inadequately treated patients with syphilis of long standing. This type of glossitis, with the secondary sheen of hyperkeratotic leukoplakia, presents a picture almost pathognomonic

of syphilis.[4] This variety of leukoplakia was recognized by the older observers and gave rise to the popular idea that leukoplakia was always of syphilitic origin. A characteristic picture of leukoplakia linguae is smooth red atrophic areas interspersed with more or less generalized leukoplakic lesions. Frequently there is a modification of the type of glossitis, and the tongue is involved in a sclerotic process with secondary lobulation, due to the contraction of interstitial connective tissue. The same surface leukokeratotic process is usually associated with this type of glossitis. In contrast to the picture presented by syphilitic glossitis is that of the reaction of the normal tongue in heavy smokers, in whom the hypertrophy and leukoplakia are confined to the papillae, producing a thick, roughened, whitish surface.

I recently had an opportunity to study at autopsy a case of carcinoma of the tongue, secondary to syphilitic glossitis (atrophic type) with secondary leukoplakia. Considerable endarteritis with narrowing

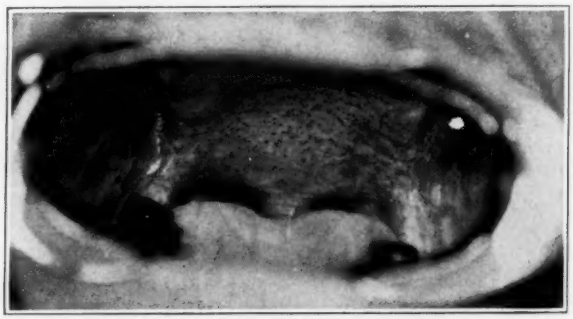

Fig. 4.—A smoker's palate, in the early stage of involvement, showing the umbilicated orifices of mucous glands.

of the lumens of the small vessels was noted. These observations suggested a reasonable theory for the production of the so-called bald tongue or syphilitic atrophic glossitis, which may be due to the following mechanism:

The tongue is an organ that may receive a heavy dose of spirochetes in the secondary stage of syphilis, with resulting endarteritis. Later, because of the interstitial sclerosing process in the patient that is inadequately treated or untreated, there results a secondary atrophy of the papillae, which are terminal epithelial tissue complexes of special function. The atrophy is undoubtedly due to the decrease in the blood supply resulting from the preexisting endarteritis. As a result of atrophy of the papillae on the dorsum of the tongue, this organ is left "naked" and exposed to irritation from the products of combustion in smokers,

4. Gastou and Trémollière: Leukoplasie linguale syphilitique, Bull. et mém. Soc. anat. de Paris **88**:49, 1903.

and other forms of irritation give rise to the protective production of epithelial plaques of leukoplakia.

The leukoplakic tissue in turn tends toward malignant growth, this explaining the high incidence of carcinoma of the tongue in patients with syphilis.[5]

Constitutional factors have been suggested as important in predisposing a person to leukoplakia or in actually causing it.

A lack of vitamin A may result in atrophy of the lingual papillae and predispose the patient to lingual leukoplakia. A hereditary predisposition to degeneration or atrophy of tissue, allied to so-called cancer susceptibility, may be a factor.

Syphilis, as has been indicated in this study, is only one factor in the development of the lingual condition, and a possible mechanism explaining the production of the condition has been described.

Fig. 5.—Atrophic syphilitic glossitis with leukoplakia of the tongue and verrucous squamous cell carcinoma of the external commissure. With electrocoagulation a five year cure was effected.

Atrophic glossitis occurs in prolonged secondary and also in pernicious anemia, probably as a result of impoverishment of the blood supply of the tongue. In such cases leukoplakia may occur independently of irritation caused by tobacco, and is a result of the use of hot or spicy food. The rare leukoplakic lesion of the tongue in women is usually secondary to the bald tongue of severe anemia.

Incidence.—Leukoplakia is overwhelmingly prevalent in men; only a small percentage of cases have been noted in women.[6] This overwhelming disparity between the sexes may change in the course of time, since women have taken up the use of tobacco, and after a number of years one might expect to see the disease more common among them.

5. Sturgis, Somers H., and Lund, Charles C.: Leukoplakia Buccalis and Keratosis Labialis, New England J. Med. **210**:996, 1934.

6. Hazen, H. H., and Eichenlaub, F. J.: Leukoplakia Buccalis, J. A. M. A. **79**:1487 (Oct. 28) 1922.

DIFFERENTIAL DIAGNOSIS

The diagnosis of leukoplakia should not be difficult, as the lesion in most cases is definite and characteristic, especially in grade 3 and grade 4 of the condition. However, there are a few conditions which simulate leukoplakia.[7]

1. Syphilitic lesions. There is a type of chronic mucous patch which presents a silvery sheen and which may resemble leukoplakia but, of

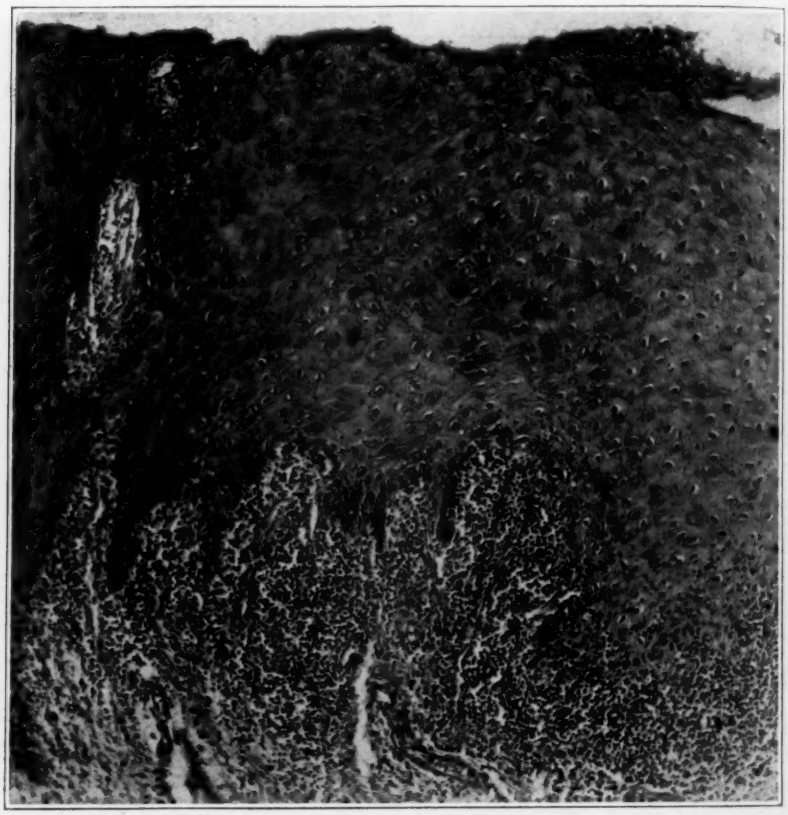

Fig. 6.—Photomicrograph of a lesion of oral lichen planus, showing decided acanthosis, slight hyperkeratosis and a sharply outlined zone of cellular infiltration; × 100.

course, is accompanied by other signs of syphilis; proper antisyphilitic treatment causes the disappearance of this lesion.

2. Lichen planus. Clinically it is difficult in certain cases of oral lichen planus, in the absence of lesions elsewhere on the body, to differentiate the condition from leukoplakia. However, in lichen planus the

7. Fox, H.: Leukoplakia Buccalis, J. A. M. A. **85**:1523 (Nov. 14) 1925.

characteristic picture is usually that of slightly raised fine papules, with dendritic whitish lesions, which tend to be symmetrical and are usually found in the buccal mucosa of both cheeks. Extensive involvement, however, may affect the tongue, particularly the lateral margins, the floor of the mouth and the lips. The two sexes are affected more or less equally with this disease. In the vast majority of cases there is an associated characteristic papular violaceous rash with angulated shiny papules involving the extremities. The microscopic picture may also be confused with that of leukoplakia, but in general in cases of lichen planus the hyperkeratotic reaction is less pronounced or even absent, and the cellular reaction of the corium is far more intense and sharply demarcated, tending to obliterate the rete cones.

3. Oral lupus erythematosus. This disease occasionally invades the lips and oral cavity by continuity from facial cutaneous lesions. The lesions usually are painful, with superficial ulceration surrounded by a zone of whitish tissue, resembling leukoplakia. They are irregularly distributed; a biopsy shows the loss of epithelial surface from the focus of ulceration and considerable cellular infiltration of the corium. Lesions which may be present elsewhere on the body help to differentiate the condition.

4. Exudative processes in the mouth. These can be differentiated from leukoplakia by the fact that the exudate can be readily removed by mechanical means, leaving a raw inflammatory surface.

COURSE OF DISEASE

The course of the disease depends entirely on the cause and on preventive and local treatment. In some cases the removal of the irritating factor, as in the occlusal and irritative group, favors the disappearance of the lesion.[8] In cases of pronounced involvement due to irritation from the use of tobacco the lesion tends to persist indefinitely but not to increase. The conditions comprising grade 1 and grade 2 have a tendency to disappear after removal of the causal factor. The symptoms of the lingual syphilitic type in which there is a preexisting atrophic glossitis, continue, and the condition has to be watched closely for evidence of a malignant lesion.

RELATION TO MALIGNANT GROWTHS

There is no question that leukoplakia is a forerunner of a malignant process.[9] It corresponds in pathologic changes to the keratotic lesion of

8. Spencer, W. G., and Cade, S.: Diseases of the Tongue, Philadelphia, P. Blakiston's Son & Co., 1931, p. 173.

9. Bloodgood, J. C.: Summary of Etiologic Factors and Resultant Lesions in Cancer of Oral Cavity, Especially in Relation to Prevention of Malignant Disease and Preservation of the Teeth, J. Am. Dent. A. **19**:1738, 1932.

the skin. The subsequent malignant growth is always of the squamous cell type, but the malignancy tends to be of low grade, making the prognosis more favorable. The ulcerative, indurated type of leukoplakia develops into a growth with the highest degree of malignancy.[10] It is difficult to demonstrate the preexisting leukoplakic lesion in a case of malignant growth, especially if the malignant growth has developed to a point where the original hyperkeratotic process cannot be demonstrated and if the patient has failed to observe the preexisting process. A malignant involvement of the tongue is preceded by syphilitic leukoplakia in a high percentage of cases. Leukoplakia of the margin of the gums due to faulty occlusion gives rise to so-called malignant disease of the jaw. Statistics on the percentage of malignant processes arising from preexisting leukoplakia are necessarily inaccurate, as in most cases the local leukoplakic lesion has been obliterated by the neoplasm.

TREATMENT

Except for the preventive form of treatment, the removal of the irritating factor in the mouth and abstinence from the use of tobacco, the treatment of leukoplakia is unsatisfactory.[11] When the use of tobacco is an etiologic factor and the patient continues to use it, the removal of the leukoplakic lesion is usually followed by a recurrence. I have used various methods of treatment in leukoplakia and have essentially given up the use of radium and of roentgen therapy, confining myself to the use of electrodesiccation and electrocoagulation by monopolar and bipolar high frequency current. I have not used the actual cautery, but I believe it is equally effective. I feel that the use of radium in the treatment of leukoplakia of the tongue associated with atrophic syphilitic glossitis is provocative of a malignant growth when the treatment is given in small doses over a long time. A malignant process has developed in 2 of my cases after this type of treatment, with the radium plaque administered in 5 mg. and 10 mg. doses for from twenty minutes to one-half hour. Treatment over months ultimately resulted in the development of processes of verrucous carcinoma. It is advisable for the physician with a patient suffering from this condition to insist that he stop all smoking, to keep him under close supervision and to use monopolar or bipolar electrocoagulation to destroy any lesion which tends toward malignant change. Multiple malignant growths of the tongue develop in this type of case, and great care

10. Bofeldt, S. A.: Pathologische anatomische und klinische Studien über die Leukoplakien der Lippen und deren Verhältnis zum Carzinom, Arb. a. d. path. Inst. d. Univ. Helsingfors **22**:325, 1927.

11. Prinz, H.: Leukoplakia Oris: A Clinical Study, Dental Cosmos **70**:663, 1928.

should be exercised in the examination of the patient. It is desirable that the patient report every few months. I have seen in a few cases a malignant process develop to an inoperable stage owing to the neglect of the patient to keep in touch with the physician or clinic. The vast majority of leukoplakic conditions require no treatment. The use of locally applied irritating or caustic remedies is contraindicated, as there is a possibility of stimulating malignant change in the lesion. The surgical removal of the malignant lesion is indicated in some cases, but I have found that in cases of leukoplakia involving the tongue this procedure is often carried to a more radical degree than necessary and the electrical current is preferable.

CONCLUSIONS

A study of 316 cases of leukoplakia is reported, with reference to the etiology and clinical gradation of the condition.

Only in cases in which the condition involves the tongue can it definitely be determined that syphilis plays a rôle in the etiology of leukoplakia.

Leukoplakia can be considered a definite forerunner of malignant growths.

Tobacco is by far the most important direct or indirect factor in the production of leukoplakia.

The mechanism involved in the production of syphilitic glossitis with leukoplakia is described.

KERATODERMA AND MELANODERMA ACCOMPANYING THERAPY WITH A GOLD COMPOUND

REPORT OF A CASE

S. IRGANG, M.D.
NEW YORK

Cases have been reported in which cutaneous hyperpigmentation appeared on the site of gold dermatitis subsequent to its resolution. There are no reports concerning the development of primary melanoderma, that is, of the spontaneous appearance of hyperpigmentation, without relation to a preexisting eruption. Likewise a search of the literature failed to reveal any reference to a concomitant production of excessive melanotic pigment in the active lesions of gold dermatitis.

It is well known that the cutaneous reactions accompanying aurotherapy are multiform. They may appear as exfoliative dermatitis or urticaria or may simulate erythema multiforme, scarlatina, lichen planus, pemphigus or pityriasis rosea. There are few references in the literature to the occurrence of keratoderma following this type of therapy, a condition which is admittedly rare.

Pardo-Castello,[1] in discussing a paper by Driver and Weller, briefly reported a case of symmetrical palmar hyperkeratosis which appeared after six injections of 50 mg. each of sodium aurothiosulfate (Möllgaard). This reaction occurred in a woman, 35 years of age, who had chronic lupus erythematosus of the face.

Rabut [2] reported a second case of keratoderma following therapy with a gold compound. The patient was a woman, aged 47, in whom exfoliative dermatitis developed after she had received nine weekly injections of allochrysin (sodium thio-auroglycerinsulfonate) of 100 mg. each for "tuberculous rheumatism." After resolution the dermatitis was replaced by melanoderma on the site of the previous exfoliative dermatitis and by a keratotic nodular eruption of the scalp, back, chest, lower extremities and mouth.

The following report concerns the development of keratoderma and melanoderma during a series of injections of gold sodium thiosulfate.

From the Department of Dermatology and Syphilology, the Harlem Hospital.

1. Pardo-Castello, V., in discussion on Driver, J. R., and Weller, J. N.: Untoward Results from the Use of Gold Compounds, Arch. Dermat. & Syph. **23**: 87 (Jan.) 1931.

2. Rabut, R.: Le keratoderma causé par l'emploi de l'or, Bull. Soc. franç. de dermat. et syph. **38**:463 (March) 1931.

REPORT OF CASE

A Negress aged 27 presented chronic superficial lupus erythematosus of one year's duration. It was limited to the nose and consisted of two plaques, the larger covering practically the entire lower third of this area and the smaller situated slightly above and to the left of the larger. There was no involvement of the oral mucosa. The patient had not been treated prior to her admission to the clinic. From July 2, 1935, to Sept. 17, 1935, she received twelve weekly intravenous injections of gold sodium thiosulfate. The dose was: for the initial injection, 10 mg.; for the second, 20 mg. and for each of the succeeding ten treatments, 25 mg. At no time did she complain of systemic symptoms that were ascribable

Fig. 1.—Secondary melanoderma of the nose (on site of previous lupus erythematosus) and primary melanoderma of the left side of the face. The hyperpigmentation of the vermilion border of the lips is not visible. The palmar aspects of both hands are decidedly thickened as the result of intense hyperkeratosis. (Photograph reproduced through the courtesy of Dr. Howard Fox.)

to an idiosyncrasy to the drug. The eruption was resolved completely after the seventh injection, that is, after the patient had received 155 mg. of gold salt. In order to prevent a relapse, treatment was continued. Pigmentation at the site of the previous lupus erythematosus appeared after the eighth injection, or after she had received 180 mg. of gold sodium thiosulfate. About this time other pigmented areas became evident on the face, particularly on the left cheek and the vermilion border of the lips. An eruption apparently due to the gold compound was first observed by the patient soon after the tenth injection, or after she had received 230 mg. of the drug. Through inadvertence two additional injections were administered; in spite of them the dermatitis was not aggravated but, on the contrary,

appeared to be slowly undergoing resolution. The patient received in all twelve injections, totaling 280 mg. of gold sodium thiosulfate.

The black discoloration of the skin was present for about five weeks. It was intense and evenly distributed throughout the entire area previously occupied by lupus erythematosus. In addition, a few small, various-sized pigmented areas appeared on the left cheek and a single spot on the right side of the nose, near the upper third. The vermilion border of the lips was evenly and intensely pigmented and slightly scaly. The melanosis also involved the mucous membrane of the lips, cheeks and hard and soft palate. On the mucous surface of the lips each pigmented area was discrete and the size of a pea. The blackish pigmentation was fairly intense and was symmetrically and diffusely distributed over the buccal mucosa

Fig. 2.—The same patient, showing symmetrical plantar hyperkeratosis. These areas are intensely pigmented as the result of excessive production of melanin in the epidermis. (Photograph reproduced through the courtesy of Dr. Howard Fox.)

and both palates. Five round whitish areas of eroded mucosa, each the size of a pinhead, likewise occurred in the mouth; two on the left cheek, one on the right, one on the lower lip and one on the gum in the region of the lower incisor teeth. The patient did not suffer from symptoms involving the mouth, such as pain, tenderness, ptyalism or a flat metallic taste. The palpebral conjunctivae were dusky and slate colored.

Dermatitis had been present for about three weeks. It was symmetrical and consisted of two types of lesions: (1) small pigmented keratotic plaques, involving chiefly the extensor surfaces of both upper and lower extremities, and (2) a diffuse pigmented hyperkeratosis, affecting both palms and soles. The keratotic plaques were roughly circular, black, firm and discrete; there was no tendency to group

or to form patches. They varied from ¼ to ½ inch (0.64 to 1.3 cm.) in diameter. Their surfaces were slightly elevated and verrucous. Intense pigmentation apparently obscured the inflammatory aspect. The lesions were not numerous; not more than a dozen were roughly scattered over each extremity. An occasional lesion was observed on the lower portion of the abdomen and on the back.

Fig. 3.—Low power photomicrograph of a section from a keratotic pigmented plaque of the leg. Note the thickened, adherent, hyperkeratotic scale which plugs into the dilated follicular orifices. The infiltrate is fairly dense and diffuse and is limited to the papillary and subpapillary layers of the corium. Note the lymphocytic infiltration invading the lower rete. Scattered through the infiltrate are chromatophores containing heavy deposits of melanin. Heavily pigmented melanoblasts may be seen in the suprapapillary rete and in other parts of the rete Malpighii.

The patient complained chiefly of thickened palms and soles, which felt leathery, and of some dulness of sensation in this area. The palmar and plantar surfaces were moderately and evenly thickened and were black and scaly. This feature

was most evident on the feet, but the discoloration of these areas was not as intense as that of the plaquelike lesions. The hyperkeratotic process was evenly distributed over these surfaces; there was no tendency to form irregular, verrucous projections, which are commonly observed after prolonged use of inorganic arsenical compounds. Pruritus, though present, was so mild that it did not appear to disturb the patient.

The Kahn test of the blood, the van den Bergh test and examination of the urine gave negative results. The icterus index was normal.

The patient was given intravenous injections of sodium thiosulfate, and local soothing applications were used. The ultimate result of treatment could not be ascertained, because the patient discontinued her visits to the clinic. She was under observation for these manifestations for only ten days, but during this period the eruption appeared to be undergoing gradual resolution. As might be expected, the pigmentation did not appear to be affected in the slightest by this therapy.

A section of tissue from a lesion on the outer aspect of the left leg was obtained for histologic study. The examination was made by Dr. T. J. Riordan, whose chief observations were as follows: There was present a profuse, laminated, adherent, hyperkeratotic scale, which plugged into the dilated follicular orifices. There was moderate, irregular acanthosis of the rete pegs. The pathologic process in the corium was limited to the papillary and subpapillary areas. The blood vessels were dilated. There was diffuse cellular infiltration, consisting mainly of round cells, young connective tissue cells and an occasional eosinophil. Wandering cells, mostly lymphocytes, invaded the lower rete in great numbers. Numerous chromatophores, containing heavy deposits of melanin, were scattered through the infiltrate. Small, dark deposits of melanin were noted in all layers of the epidermis.

COMMENT

There is no doubt that gold as well as arsenic is capable of stimulating the epidermal cells to proliferation and to excessive pigment formation. Pigmentation following the administration of inorganic arsenical compounds occurs only after prolonged use and is characterized clinically by a reticular or mottled appearance. Melanoderma following treatment with an organic compound of arsenic or gold appears in a comparatively short time and is distributed evenly in patches of variable size. There are, however, exceptions to this rule. Gougerot and Carteaud [3] reported a case of hyperpigmentation of the reticular variety, which appeared after the resolution of gold dermatitis and which was limited to the areas previously occupied by the eruption.

Pigmentary changes merit serious consideration not only because of their tendency to persist indefinitely but also because of their disfiguring effect. The Negro race is more prone to hyperpigmentary disturbances than any other; furthermore, when such a disturbance does appear in a Negro, it is apt to be more intense than in a white person. As might be expected, melanoderma following arsphenamine therapy occurs more frequently in the Negro. It may develop on any part of the body, but it is most common on the cheek, vermilion border of the lips and buccal

3. Gougerot, H., and Carteaud, A.: Pigmentation réticulée survenue après une érythrodermie aurique, Bull. Soc. franç. de dermat. et syph. **38**:47 (Jan.) 1931.

mucosa. This reaction of the Negro skin to therapy with a gold compound unrelated to a preexisting dermatitis must be relatively rare, for it has never been previously observed in a clinic which is comprised chiefly of Negro patients. This observation also applies to the development of intense melanotic pigmentation in active lesions.

While it is not unusual for the arsphenamines to produce melanoderma in the Negro, they rarely cause keratoderma. Except for the two cases cited of keratoderma following therapy with a gold compound, no reference to this subject has been found.

In a hypersensitive person comparatively small doses may cause an unfavorable reaction. In the case under discussion the cutaneous changes became evident after the patient had received only eight weekly intravenous injections of a gold salt, with an average dose of 22.5 mg.

SUMMARY AND CONCLUSIONS

A case is presented in which unusual cutaneous reactions followed treatment with comparatively small doses of gold sodium thiosulfate. The patient was a Negress who had suffered from chronic lupus erythematosus for one year.

Melanoderma became evident after the eighth weekly injection, or after she received 180 mg. of gold salt, the average dose being 22.5 mg.

Keratoderma and mild stomatitis appeared after the tenth weekly injection, or after the patient received 230 mg., the average dose being 23 mg.

There were no systemic evidences of hypersensitiveness to this compound.

Histologic examination showed the epidermis and the papillary and subpapillary layers of the corium to be involved in the allergic reaction. In the epidermis the effect was stimulating, increasing cellular proliferation and exciting the special pigment cells to an increase in activity. In the corium its irritating effect manifested itself in dilatation of the blood vessels, slight edema, infiltration of round cells and proliferation of young connective tissue cells.

The histologic picture was suggestive of lupus erythematosus, but the clinical appearance of the lesions and history of the case eliminated this diagnosis

It is the consensus that the allergic cutaneous reactions to gold and to arsphenamine compounds are similar in appearance. A cutaneous involvement following the use of organic arsenicals is undoubtedly more frequent than that following treatment with a gold compound.

The Negro race is the most susceptible to pigmentary disturbances. Primary melanoderma following aurotherapy has never been observed before in this clinic, in which most of the patients are Negroes.

Keratoderma rarely follows therapy with a gold compound, only two similar conditions having been recorded.

FUSOSPIRILLARY GANGRENOUS STOMATITIS

ELMORE B. TAUBER, M.D.
AND
LEON GOLDMAN, M.D.
CINCINNATI

Ever since Richter's report in 1828 entitled "Das Wasserkrebs der Kinder," numerous reports have appeared relative to this particular syndrome. In the descriptions of many of the early cases, noma was considered as a clinical entity. This, however, is not true. It is merely a type of necrotic ulceration of selective localization and of varied etiology. Gangrenous stomatitis is only one form of noma. Rasskina-Braude and Jordan and Ryndik [1] listed the following characteristics of noma: (1) onset with ulceration of the mucous membrane, which rapidly assumes a gangrenous character and becomes grayish black; (2) edema and swelling, with central infiltration; (3) extension of the process to the adjacent skin, first with a crust and later with perforation under this crust; (4) exposure and necrosis of neighboring bones and loosening and eventual loss of teeth; (5) severe pain and a tendency to bleeding; (6) characteristic gangrenous odor; (7) secondary occurrence; (8) rapid spread of the process, with frequently a fatal end; (9) localization of the lesion not only around the mouth, but around the other orifices of the body—ears, nose, vulva; (10) debilitation, and (11) unilateral tendency of the infection.

There seems to be some difference of opinion as to the etiology. Many believe that it is caused by either a fusospirillary infection (Plaut [2] and Vincent [3]), diphtheria [4] or a type of staphylococcus-streptococcus symbiosis. It seems that under the influence of some systemic infection or reaction the saprophytes usually present in these particular orificial areas become violently pathogenic. The condition is more common in children and occurs more frequently after measles [5] than after the other

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From the Department of Dermatology, Cincinnati General Hospital of the College of Medicine of the University of Cincinnati.

1. Jordan, A., and Ryndik, R.: Noma oder nomaähnliche Gangrän? Arch. f. Dermat. u. Syph. **169**:341, 1933.

2. Plaut, H. C.: Studien zur bacteriellen Diagnostik der Diphtherie und der Anginen, Deutsche med. Wchnschr. **20**:920, 1894.

3. Vincent, H.: Sur l'étiologie et sur les lésions anatomo-pathologiques de la pourriture d'hôpital, Ann. Inst. Pasteur **10**:488, 1896.

4. Repetto, E.: Contributo clinico allo studio del noma, Riforma med. **124**:132, 1933.

5. Vertán, E.: Uber einen Fall von Noma vulvae, Zentralbl. f. Chir. **58**:2390; 1931.

contagious diseases. Noma is much less frequent at the present time than it was formerly.

The few reports available of the occurrence of the condition in an adult reveal evidence of systemic disturbance as a predisposing factor. "Pronounced arteriosclerosis or some slight trauma, as the extraction of a tooth, may be the starting point of noma in debilitated old people." [6] Among the few reported cases in adults is that of Rodelius and Steyer [7] whose patient, a 43 year old woman, had a condition which started with gangrenous ulceration around the gum and was followed by involvement of the antrum. Death occurred as a result of purulent meningitis. Jedlička, Václav and Horničlk [8] reported a case in a 35 year old woman with chronic nephritis and myocarditis, in whom noma developed after aphthous stomatitis. Postmortem examination revealed gangrene of the lungs, with organisms of various types scattered throughout the tissues.

The case reported here is the first observed in an adult at the Cincinnati General Hospital. A few cases have been observed by the pediatric staff of the contagious service.

REPORT OF A CASE

L. G., a white woman 37 years old, married, was admitted to the dermatologic service complaining of a sore in her mouth. This began one month prior to her admission, with a painful ulceration underneath the tongue. In spite of local treatment and three intravenous injections by her attending physicians, the lesion continued to spread. Shortly before her admission, edema of the ankles and a gradually increasing effort dyspnea began to develop.

When the patient was 23 years old, she was told she had "heart trouble" following rheumatism. Ten years prior to her admission to the hospital, she was ill, with numerous red, tender joints, and ever since that time, she had taken active treatment for her cardiac condition. There was no history, either personal or familial, of syphilis or tuberculosis.

Examination on admission revealed a chronically ill white woman, who appeared very uncomfortable. She was sluggish in her responses but fully oriented. There was cyanosis of the lips and nail beds. The skin was pale, clear and elastic. General examination showed evidence of mitral stenosis, with auricular fibrillation, bilateral hydrothorax and edema of the lower extremities. There was a marked fetor ex ore. There were no teeth. The gums were somewhat cyanotic and clear. The floor of the mouth underneath the tongue was covered by a foul-smelling bluish-black necrotic area about 4 by 6 cm. A slight amount of oozing occurred when any portion of the slough was removed. No masses were palpable. The remainder of the pharynx was clear. Save for marked edema of the labia, the vaginal examination gave entirely negative results.

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6. Prinz, Hermann, and Greenbaum, Sigmund S.: Diseases of the Mouth and Their Treatment, Philadelphia, Lea & Febiger, 1935.

7. Rodelius, E., and St. Steyer: Ein Beitrag zur Frage der nomaähnlichen idiopathischen Stomatitis gangrenosa (akute Mundgangrän), Beitr. z. klin. Chir. **148**:476, 1930.

8. Jedlička, V., and Horničlk, V.: Stomatitis und Glossitis gangrenosa, Zentralbl. f. Haut- u. Geschlechtskr. **44**:192, 1933.

The white cell count was 8,200, with 72 per cent polymorphonuclears, 3 per cent eosinophils, 23 per cent lymphocytes and 2 per cent mononuclears. Several repetitions of this differential count showed no essential changes. The red cell count was 3,600,000, with 70 per cent hemoglobin. The urine was normal save for transient albuminuria. Smears from the floor of the mouth showed numerous fusiform bacilli and spirillas. A few cocci were also present. No diphtheria bacilli were found in culture. The Kahn reaction was negative.

The patient used neoarsphenamine in glycerin and sodium perborate locally for a few days, and at that time she took various diuretics and repeated doses of digitalis. The congestive heart failure improved rapidly. The condition in the mouth spread quickly in spite of various forms of local therapy. The administration of neoarsphenamine intravenously was started ten days after her admission, and she received a total of 3 Gm.

The local therapy consisted of sodium perborate, hydrogen peroxide, potassium permanganate, mapharsen (the hydrochloride of meta-amino-para-hydroxyphenylarsine oxide), sodium ricinoleate solution, bismuth pastes and benzoyl peroxide powder. The systemic treatment, in addition to neoarsphenamine, included repeated small blood transfusions and intravenous injections of a 50 per cent solution of dextrose.

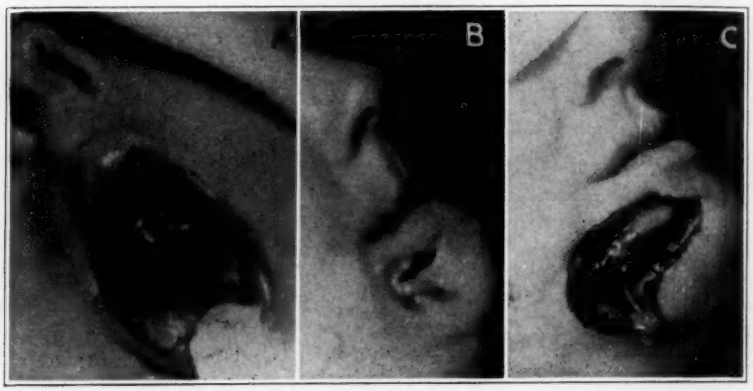

Fig. 1.—*A*, necrotic area, under the tongue at the time of the patient's admission to the hospital. *B*, the lesion shortly after the perforation of the gangrenous stomatitis through the chin. *C*, extent of the gangrenous ulceration of the tongue, the floor of the mouth and the chin shortly before death.

In spite of all these measures, the necrotic ulceration continued to spread, involving the entire floor of the mouth and a portion of the tongue. The mucous membrane of the lower lip was likewise involved, and overnight, perforation occurred through the lower lip. This gangrenous slough spread rapidly throughout the skin. At that time, the fusiform bacilli and spirilla were found repeatedly, both organisms in abundance. These organisms were found also on the edge of the gangrenous cutaneous slough. Culture at that time showed only hemolytic streptococci, Bacillus coli, staphylococci and a yeast, apparently a saprophyte. Tissue culture for a streptococcus-staphylococcus symbiosis (Dr. Longacre) showed no special organisms. Bleeding from the lesion was difficult to control at times. An attempt at gentle débridement forty-eight days after admission was followed by

oozing, which could not be controlled by any local measures. In spite of various types of restoratives, the patient died ten hours after this débridement.

Postmortem examination two hours after death showed extensive endocarditis, with mitral stenosis and chronic passive congestion of the viscera, aortic and coronary atherosclerosis and hypertrophic cirrhosis of the liver. The posterior part of the pharynx showed no ulceration, and the entire tracheobronchial tree was free from ulceration. The intestines were normal. Microscopic sections of the gangrenous areas showed irregular areas of necrosis (no "three zone type") associated with polymorphonuclear and lymphocytic exudates and occasional giant cells. In the superficial portions of the ulcerated areas cocci were the only organisms identified. No spirilla were noted on smears made post mortem. Special silver stains of the tissues were not made.

COMMENT

In this patient, then, the gangrenous stomatitis developed under the influence of an old rheumatic heart disease with a recent phase of congestive failure. It is rather difficult to assign any particular systemic factor as being responsible for the development of the gangrenous stomatitis, because cirrhosis of the liver and congestive heart failure have occurred in numerous persons with dirty, infected mouths, and these patients did not acquire gangrenous stomatitis. Chronic infection of the mouth has been shown before [9] to be an important factor in the subsequent development of severe and even fatal fusospirillary infection. In this instance, then, one can say only in a general fashion that the systemic disturbances were in favor of the development of this type of gangrene. Even after the congestive failure was relieved, the patient showed no improvement because the process had already extended too far. An attempt was made to evaluate various organisms found locally on the affected tissue, but the studies made by Dr. Longacre [10] on the staphylococcus-streptococcus symbiosis showed nothing conclusive, and fusiform bacilli and spirilla were found in great abundance during the entire period of observation. In spite of the controversy concerning the fusospirillary etiology of infections of the mouth, one must say in this case that these organisms were associated constantly with the gangrenous tissue and were probably causal agents.

This case shows also the inadequacy of all forms of local and even systemic therapy. This observation was noted before [9] in instances of fatal extensive fusospirillary infection. The question of surgical intervention, of course, is always considered, and in this case the mild attempts at débridement were responsible for hastening the inevitable death of the patient. One may generalize and say that early in the course of the disease, if the infection shows no immediate response to

9. Goldman, Leon, and Kully, Herman E.: Fatal Fusospirochetal Angina, J. A. M. A. **101**:358 (July 29) 1933.

10. Longacre, J. J.: Personal communication to the authors.

therapy, radical measures should be considered, since, as Jordan and Ryndik [1] claimed, "in over one half of the cases death ensues." Prinz and Greenbaum [6] went so far as to say that "from 70 to 80 per cent of all cases end fatally in a very short time.

SUMMARY

A case is reported of gangrenous stomatitis with perforation through the chin occurring in a 37 year old woman. In spite of all forms of therapy, fusiform bacilli and spirilla in great abundance were found in the tissues. The patient had also old rheumatic heart disease, with congestive failure and cirrhosis of the liver. Postmortem examination showed the localization of the gangrenous process to the buccal cavity and the chin.

PEMPHIGUS VULGARIS OF THE ERYTHEMA MULTIFORME VARIETY

OSCAR L. LEVIN, M.D.

JESSE ALFRED TOLMACH, M.D.
AND
JOEL SCHWEIG, M.D.
NEW YORK

While pemphigus vulgaris is a clearly defined clinical entity, the course of the acute variety is still a matter of conjecture. In his thorough study of the subject, Riecke,[1] as late as 1931, left open the question of the nosology of the condition. Ehrmann[2] stated that when pemphigus is ushered in by erythema multiforme, not only is the prognosis rendered unfavorable but the course of the disease is shortened and the fatal outcome occurs sooner. In dealing with erythema multiforme bullosum, one is often baffled at the onset by inability to determine its etiology and its prognosis. The subsequent development of pemphigus is not frequent and deserves careful investigation. With these considerations in mind, we are reporting a case which presented some interesting features.

REPORT OF A CASE

L. H., a 70 year old Polish Jew, lived in the United States for thirty-seven years. Until his retirement five years previously he had been employed in the dairy business. Nothing of importance was brought to light from the family history. The patient had no knowledge of the occurrence of a bullous eruption among his relations. Except for the presence of cataracts and hemorrhoids the patient had never been sick until the present illness.

Two weeks prior to his admission to the Beth Israel Hospital, on Oct. 12, 1934, an eruption developed; it came on suddenly and, with the exception of the face, spread quickly over the whole body. It was preceded by a generalized feeling of illness, accompanied by chills, headache and nausea. The eruption consisted of urticarial lesions, which turned shortly into blisters and caused severe itching. There was no history of the ingestion of drugs. At the time of the onset of the eruption the patient was suffering from an infected toe which did not cause much discomfort and to which a salve had been applied.

Physical examination revealed an old man, in generally good condition. His hearing was slightly impaired; there was a cataract on the right eye, and the

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From the Department of Dermatology and Syphilology, the Beth Israel Hospital.

1. Riecke, E.: Pemphigus, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, chap. 2.

2. Ehrmann, S.: Vergleichend-diagnostischer Atlas der Hautkrankheiten und der Syphilide, Jena, Gustav Fischer, 1912, p. 150.

sequelae of an iridectomy were noted in the left eye. The right pupil reacted to light and in accommodation, but the left was fixed by adhesions. The chest was emphysematous. The upper and lower extremities were swollen, though the feet were surprisingly free from edema. The heart and lungs as well as the gastrointestinal and the urogenital tract were normal.

Cutaneous examination revealed an acute inflammatory eruption, covering the entire body with the exception of the face and scalp. The lesions were vesicular and bullous. Each was situated on an inflamed base and surrounded by a hyperemic ring; they ranged in diameter from 1 to several centimeters. A fetid odor emanated from denuded areas, which were produced by the rupture of the larger bullae. The contents of the bullae, which varied according to the stage of development of the lesions, appeared at first to be clear and later seropurulent. On the toes the contents of the bullae were hemorrhagic. The mucous membranes were normal, except that there was one large bulla on the hard palate. Through coalescence of bullae on the trunk as well as on the extremities, polycyclic figures had formed. Rupture of the bullae resulted in moist areas, with tense, bulging margins. The lesions were tender on palpation.

The eruption improved gradually under local bland therapy, general hygienic measures and intramuscular injections of sodium arsenite. But the improvement was temporary, since at regular intervals a new crop of lesions with similar characteristics appeared.

In the seventh week of illness, there was a definite change in the eruption. Bullae appeared on apparently normal skin. The underlying skin showed no erythema and had lost its inflammatory character. The bullae, however, were more purulent and had a more offensive odor.

From the appearance of the eruption at this time, the diagnosis of pemphigus vulgaris was readily established. The Nikolsky sign, which had been negative at the onset, was now definitely positive. The temperature was normal.

Laboratory examination revealed that the urine had a specific gravity of 1.020 and contained numerous phosphates, a few red blood cells and a trace of albumin. The blood count showed 5,000,000 red cells and from 18,000 to 24,000 white cells per cubic millimeter. The hemoglobin content was 96 per cent (Sahli). The differential count was as follows: 85 per cent polymorphonuclear neutrophils, 10 per cent monocytes and 5 per cent eosinophils. The chemical examination of the blood revealed 33 mg. of dextrose per hundred cubic centimeters. There were gram-positive and gram-negative bacilli in the feces. Staphylococcus aureus was observed microscopically in the contents of the bullae. The phytopharmacologic test (Pels-Macht) showed an index of 61 per cent, which indicated a highly toxic state.

During the eighth week of the disease the temperature rose to 103 F. The patient gradually became weaker, and one week later, or two and one-half months after the onset of the illness, he died of hypostatic pneumonia.

DIFFERENTIAL DIAGNOSIS

At first the diagnosis of erythema multiforme exsudativum bullosum was suggested by the following symptoms: the symmetrical arrangement of the lesions, which favored the upper and lower extremities; the bullae, which appeared on an inflamed base and were surrounded by an erythematous border; the tendency of the lesions to form configurations, and the outstanding subjective complaints. However, that diagnosis was

eliminated when we considered the course of the disease in the four weeks before the patient's death and the disappearance of the erythema, the return of the temperature to normal, the positive Nikolsky sign, the fact that the bullae arose on apparently normal skin, the large denuded cutaneous surfaces, with the offensive odor, and the lethal ending.

A bullous drug eruption, such as may be produced by iodides, bromides or antipyrine, was excluded since the test of the urine for the suspected drug gave negative results and since there was no history of the ingestion of drugs. A drug eruption usually appears as a localized or as a generalized diffuse erythema, which only occasionally presents vesicular and bullous lesions and rarely causes death.

Dermatitis herpetiformis (Duhring) presents a different picture. The lesions are polymorphous and show a characteristic configuration. The general appearance of the patient is usually good; there is no fever, and the pruritus is intense. Though at times dermatitis herpetiformis closely resembles pemphigus and erythema multiforme, it can be distinguished from these by its chronic eruption, the intense itching and the history and behavior of the disease. Variola and epidermolysis bullosa acquisita were dismissed from consideration.

Pemphigus acutus infectiosus, sometimes called butcher's pemphigus, of Pernet because of the prevalence of the infection among butchers and others who deal with animals, is seen in patients who have suffered definite injury with contamination by infectious material before the outbreak of the eruption. The blebs, which develop within two weeks or a month after the injury, usually are centered around the wound. Because of its distinct features and its favorable prognosis this condition is easily recognized and can be distinguished from pemphigus.

COMMENT AND CONCLUSION

A fatal case of pemphigus vulgaris of short duration, ushered in by erythema multiforme bullosum, is described. The symptoms and the course of the eruption, with its unknown etiology, pointed to pemphigus; therefore, the following questions arose: Is there an identity of pemphigus vulgaris with erythema multiforme bullosum? Is there an actual development of a separate disease ensuing from a primary one of a different nature? Finally, is there a mutation from one disease to another? These questions will persist as long as the etiology of erythema multiforme bullosum and of kindred diseases remains unknown. The contributions to the literature supporting one hypothesis or the other are too numerous to be cited. We believe with Ehrmann that the concept of pemphigus vulgaris should be broadened to include the erythema

multiforme variant. Grouven [3] expressed the opinion that it is entirely plausible that the hypothetic causative agent of pemphigus vulgaris may sometimes strike suddenly and exhaust itself in a single fatal attack. Pels and Macht [4] stated the opinion that a patient with erythema multiforme bullosum who shows persisent toxicity of the blood should be regarded as having potential pemphigus. Since one is unable to determine the outcome of erythema multiforme bullosum, the prognosis of this condition must be guarded.

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3. Grouven, C.: Der Pemphigus chronicus in seinen Varietaeten, Arch. f. Dermat. u. Syph. **55**:85, 1901.

4. Pels, I. R., and Macht, D. I.: Phytopharmacologic Test in Dermatology, Arch. Dermat. & Syph. **29**:214 (Feb.) 1934.

FAILURE TO DEMONSTRATE SPIROCHAETA PALLIDA IN CEREBROSPINAL FLUID OF SYPHILITIC CHINESE PATIENTS

L. PEARCE, M.D.

C. K. HU, M.D.

AND

J. W. MU, M.D.

PEIPING, CHINA

The demonstration of Spirochaeta pallida in the cerebrospinal fluid of syphilitic patients has been successfully accomplished many times, but the frequency with which organisms may be found is still uncertain. The general impression seems to be that the incidence is comparatively high; this is probably due to the fact that positive rather than negative results have attracted attention. Few series, moreover, are sufficiently large to permit statistical evaluation of results. The matter is further complicated by the fact that various technics have been employed. At present, at least, only one, that of inoculation of animals, gives any information as to the important point of the viability of the organisms.

The majority of investigations on this aspect of syphilitic disease have been carried out on white and Negro patients in European and American clinics. In 1931 and 1932 a study was made on the cerebrospinal fluids of forty Chinese patients in Peiping by the method of inoculation of rabbits, the results of which are reported in this paper. The failure to demonstrate organisms in any of these cerebrospinal fluids is of particular interest in view of the opinion held by some observers that there are differences in the clinical manifestations of syphilis in the Occident and in the Orient.

DATA ON PATIENTS FORMING THE BASIS OF THIS STUDY

The cerebrospinal fluids of forty-two patients were studied. Forty patients were Chinese, one was an Armenian and one a Pole. Thirty-seven of the patients were males; four Chinese and the Polish patient were females. The mean age for the total series was 32 years; eight patients were 40 or more years of age, while the mean age of the others was 28. As is shown in tables 1 and 2, twenty-five patients had not been treated. With one exception, to be noted later, the amount of treatment received by seventeen patients was almost negligible. Arsphenamine, a preparation of bismuth, mercury and, occasionally, neoarsphen-

From the Division of Dermatology and Syphilology, Department of Medicine, Peiping Union Medical College.

amine were the drugs used in treatment referred to as "injection." Of seventeen patients the great majority had received but one, two or three injections at variable periods before lumbar puncture was performed. In the case of two patients the intervening period was four and five days, respectively, but in that of the others it was from one month to seven years.

Observations on twenty-four patients are recorded in table 1.

The Wassermann reaction of the blood of all these patients was positive. There were twenty-three patients with secondary syphilis of the skin and bones, in six of whom a chancre was still present, and one patient had iridocyclitis (table 1). The duration of the disease in nineteen patients was from one to eight months; in five patients it was from one to two years. The duration of the symptoms ranged from ten days to six weeks in fourteen patients; in the remainder it was from two to seven months. Fourteen patients had not been treated (table 1). Of the ten patients who had been treated (table 1), only one had received more than three injections; one patient had been given one injection five days before lumbar puncture was performed, but the others had not been treated for at least one month. The cerebrospinal fluids of most of the twenty-four patients were normal. In six fluids the cell count exceeded 4 cells per cubic millimeter, the highest counts being 10 and 12 cells; in seven the total protein content as determined by Ling's method [1] slightly exceeded 50 mg. per hundred cubic centimeters, and the Wassermann reaction of one fluid was positive.

Observations on eighteen patients are recorded in table 2.

There were three patients with an early stage of diffuse meningitis. The duration of the infection was reported to be one month, one and a half years and eight years, while the duration of the present symptoms was two weeks, one month and six months, respectively. One patient had a chancre, another had a papular rash and mucous patches. One patient had been given two treatments seven years previously; the others had not been treated. The fluids of two patients with an early stage of diffuse meningitis showed a positive Wassermann reaction; in the fluids of all three of them the cell count was increased, and in the fluids of two the protein content was slightly increased.

There were five patients with neurorecurrence affecting the eighth cranial nerve, and in one of these the second nerve was also involved (table 2). One patient had suffered from deafness (neurorecurrence) seven years before the present admission and had received thirty-seven injections of neoarsphenamine, mercury and a bismuth preparation at that time. The other patients with neurorecurrence had been given from one to six treatments; one had been treated four days before lumbar puncture was made, but the others had been treated from three months to five years previously. Two patients had a macular or papular rash, and a third had mucous patches. The number of cells in the cerebrospinal fluids of the five patients with neurorecurrence was 5, 7, 12, 28 and 42 per cubic millimeter, respectively. The total protein content of three fluids was slightly increased. One fluid showed a positive Wassermann reaction, but dark-field examination of a centrifugated portion of that fluid gave negative results.

Of five patients with tertiary syphilis (table 2) one had aortic insufficiency; one, aortic aneurysm; one, cutaneous gumma and periostitis; one, keratitis and bursitis, and one, periostitis and alopecia. In these patients the duration of the disease was reported as ranging from four to twenty years, and that of the present symptoms, from three months to three years. Only one patient had been treated, and the treatment had consisted of a single injection given one month

1. Ling, S. M.: J. Biol. Chem. **69**:397, 1926.

TABLE 1.—*Observations on Patients not Showing Evidence of Involvement of the Nervous System*

Case Number	Duration of Disease	Symptoms	Period of Hospitalization	Treatment: Number of Injections	Treatment: Time Between Last Injection and Lumbar Puncture	Observations on Cerebrospinal Fluid: Wassermann Reaction	Observations on Cerebrospinal Fluid: Number of Cells per Cu.mm.	Observations on Cerebrospinal Fluid: Total Protein Content, Mg. per 100 Cc.	First Animal Passage: Number of Rabbits	First Animal Passage: Number of Blood Examinations	First Animal Passage: Period of Observation, Days	Interval Between Inoculations, Days	Second Animal Passage: Number of Rabbits	Second Animal Passage: Number of Blood Examinations	Second Animal Passage: Period of Observation, Days
1	1 mo.	Papular rash, chancre.....	1 wk.	None	.....	—	—	54	2	7	148	61-132	4	7	83-150
2	2 mo.	Papular rash, chancre.....	2 wk.	None	.....	—	3	+	1	4	86	86	1	2	121
3	1 mo.	Macular rash, chancre.....	10 days	None	.....	—	3	+	1	5	94	94	2	4	127
4	2 mo.	Macular rash, chancre.....	?	None	.....	—	10	?	2	3	87	87	2	2	98-123
5	?	Macular rash, chancre, arrhythmia.....	?	None	.....	—	5	?	2	2	79	79	2	..	188
6	2 mo.	Papular rash.....	2 wk.	None	.....	—	2	55	2	3	93	93	1	..	123
7	?	Papular rash, arrhythmia.	6 wk.	None	.....	—	—	—	2	3	94	94	2	1	204
8	3 mo.	Papular rash, headache, arrhythmia.....	7 wk.	None	.....	—	2	+	2	3	85	85	2	2	132
9	2 mo.	Papular rash.....	12 days	None	.....	—	2	—	2	3	98	98	2	2	212
10	2 yr.	Follicular rash.....	5 mo.	None	.....	—	6	+	2	..	100	..	..	..	...
11	4 mo.	Condyloma.....	6 wk.	None	.....	—	—	—	2	2	77	77	2	..	170
12	8 mo.	Condyloma.....	2 wk.	None	.....	—	*	?	1	3	82	82	2	1	182
13	1 yr.	Condyloma, alopecia.....	4 wk.	None	.....	—	—	51	2	..	104	..	..	..	...
14	?	Condyloma.....	2 wk.	None	.....	—	6	—	2	1	114	81	2	..	130
15	18 mo.?	Periostitis, chancre.....	2 mo.	2	2 mo.	+	?	+	2	3	102	102	2	2	108-188
16	1 mo.	Papular rash.....	2 wk.	1	5 days	—	3	60	2	2	79	79	2	..	188
17	2 yr.	Condylomas.....	2 mo.	1	2 yr.	—	8*	+	2	6	84	84	2	3	130
18	?	Condylomas.....	2 mo.	3	1 yr.	—	8	56	2	..	105	105	2	..	45-50
19	11 mo.	Papular rash, periostitis...	2 wk.	7	4 mo.	—	4	—	1	3	100	100	2	1	108
20	2 yr.	Periostitis.....	7 mo.	2	2 yr.	—	3	52	1	1	119	119	2	—	104
21	4 mo.	Papular rash, alopecia.....	2 wk.	3	1 mo.	—	1	49	2	6	86-165	86	1	4	135
22	4 mo.	Condylomas, alopecia.....	6 wk.	1	4 mo.	—	2	56	2	2	82	82	2	4	136
23	7 mo.	Iridocyclitis.....	1 wk.	2	7 mo.	—	12	48	2	2	204	77	2	..	130
24†	?	Periostitis.....	4 mo.	1	1 mo.	—	2	—	2	3	83	83	2	1	185

* The fluid was blood tinged.
† This patient was a Pole.

TABLE 2.—*Observations on Patients with Involvement of the Nervous System or with Tertiary or with Latent Stages of Syphilis*

Case Number	Duration of Disease	Symptoms	Period of Hospitalization	Treatment: Number of Injections	Treatment: Time Between Last Injection and Lumbar Puncture	Observations on Cerebrospinal Fluid: Wassermann Reaction	Observations on Cerebrospinal Fluid: Number of Cells per Cu.mm.	Observations on Cerebrospinal Fluid: Total Protein Content, Mg. per 100 Cc.	First Animal Passage: Number of Rabbits	First Animal Passage: Number of Blood Examinations	First Animal Passage: Period of Observation, Days	Interval Between Inoculations, Days	Second Animal Passage: Number of Rabbits	Second Animal Passage: Number of Blood Examinations	Second Animal Passage: Period of Observation, Days
		Early Stage of Diffuse Meningitis													
25	1 mo.	Headache, chancre	1 mo.	None	.....	—	35	52	2	6	88	88	2	1	174
26	18 mo.	Headache, papular rash, macular patches	6 mo.	None	.....	+	+*	56	2	6	193	102	2	2	188
27	8 yr.?	Headache	2 wk.	2	7 yr.	+	700	?	1	3	187	100	2	1	170
		Neurorecurrence													
28	4 mo.	Involvement of 8th cranial nerve, macular patches	2 wk.	1	3 mo.	—	12	52	2	..	68	68	2	..	170
29	?	Involvement of 8th cranial nerve	?	6	4 days	—	5	56	2	3	81	81	2	1	127-185
30	4 mo.	Involvement of the 8th and 2d cranial nerves	1 mo.	2	3 mo.	+	7	+	1	2	85	85	2	..	188
31	3 yr.	Involvement of 8th cranial nerve, papular rash, condylomas	2 yr.	1	3 yr.	—	28	52	2	1	74	74	2	..	170
32	8 yr.	Involvement of 8th cranial nerve, macular rash, arrhythmia	7 yr.	37	5 yr.	—	42	49	2	1	196	125	2	..	100
		Tertiary Syphilis													
33	4 yr.?	Aortic insufficiency	2½ yr.	None	.....	—	3	51	2	2	94	94	2	1	105
34	20 yr.	Aortic aneurysm	3 yr.	None	.....	—	2	+	2	1	119	119	2	..	104
35	13 yr.	Cutaneous gumma, periostitis (2 wk.)	6 mo.	None	.....	—	4	52	2	2	79	79	2	..	173
36	7 yr.	Keratitis, bursitis (3 mo.)	2 yr.	None	.....	—	2	47	2	1	70	70	2	..	170
37	2-4 yr.	Periostitis, alopecia	1 yr.	1	1 mo.	—	4	55	2	3	83	83	2	1	186
		Late Stages of Latent Syphilis													
38	7 yr.	.....	.....	None	.....	—	2	51	1	2	83	83	2	1	182
39	12 yr.?	.....	.....	None	.....	—	2	?	2	8	105	89	2	2	113-133
40	6 yr.	.....	.....	None	.....	—	—	56	2	1	103	103	2	..	104
41	12 yr.	Diminished reflexes	.....	None	.....	+	70	56	2	5	95-105	95	1	1	174
42†	20 yr.	Asymptomatic involvement of the central nervous system	.....	None	.....	+	642	++	2	2	190	107	2	..	104

* The fluid was blood tinged.
† This patient was an Armenian.

previously. The spinal fluids of all the patients with tertiary syphilis were normal except for the fact that three specimens showed slightly high values for the total protein content.

The last group of five patients (table 2) comprised three with latent syphilis, one with questionable tabes and one with asymptomatic neurosyphilis. The duration of disease was from six to twenty years. None of them had been treated. The spinal fluids of the patients with latent syphilis were practically normal. The fluids of the other two showed a positive Wassermann reaction, an increased cell count and an increased value for the total protein content. The colloidal gold curve and the mastic curve of the fluid of the patient with questionable tabes were normal.

EXPERIMENTAL PROCEDURE

Within a few minutes after the fluid was withdrawn, each of the forty-two fluids, without being centrifugated, was injected into one or both of the testicles of normal adult rabbits. Each of thirty-five fluids was tested on two rabbits and each of seven fluids, on one rabbit, a total of seventy-seven animals being used. The amount of fluid available after the removal of a portion for other tests determined whether one or two animals were used. In the majority of cases from 1 to 2 cc. was injected into each animal; a few received 0.75 cc. The rabbits were kept under observation for an average of three and one-third months, the majority being observed for at least three months; the longest period of observation was two hundred and four days and the shortest sixty-eight days.

A second animal passage was carried out in forty cases; that is, the test was repeated with material derived from the rabbits which had received forty of the forty-two fluids.

The mean interval before the second passage was three months after the injection for the first passage. The longest interval was one hundred and twenty-five and the shortest sixty-one days, respectively; in only seven cases was the interval less than eighty days. The material used for inoculation was an emulsion of both popliteal lymph nodes in saline solution, nodes from both or from only one of the originally inoculated animals being used. For ten transfers the nodes were removed surgically with the animal under ether anesthesia, and the rabbit was kept under observation for a variable period thereafter. For thirty transfers the rabbit was killed by an injection of air into a marginal vein of the ear, and the nodes were removed aseptically. A small amount of a comparatively thick emulsion was prepared so that all the material from the nodes could be used. In three instances portions of the originally inoculated testicle were included in the emulsion. The inoculations were made intratesticularly in normal rabbits, the average dose for each animal being 1 cc.

For the second animal passage a total of seventy-eight rabbits received injections, thirty-five emulsions being tested on two, four on one and one on four rabbits. The animals were observed for a mean interval of one hundred and seventy days; seventy-five were followed for from one hundred to two hundred and four days, while three were observed for forty-five, fifty and eighty-three days, respectively.

In one instance a third animal passage was carried out. The popliteal lymph nodes of two rabbits used for the second passage were removed one hundred and four days after the animals had been inoculated. The emulsion was injected intratesticularly in two normal rabbits which were observed for one hundred days.

All the rabbits were carefully examined clinically at least twice a week for local and general evidence of infection. Examination always included palpation of the testicles, whether inoculated or not, and of the popliteal lymph nodes. In

instances in which the presence of pathologic changes in the testicles was suspected, aspirated testicular fluid was examined microscopically by the dark-field method.

Wassermann, Kahn and Kline tests were made on the blood serums of the majority of the rabbits. In ascertaining the results of the first passage, these tests were made on the serums of the animals inoculated with thirty-eight of the forty-two fluids. The number of examinations of the blood per set of animals representing each fluid varied from one to eight, the average being three examinations. In determining the results of the second passage tests were carried out on twenty-three of the forty sets of inoculated rabbits. From one to seven tests were made, the average being two tests on each set of rabbits.

At the end of the period of observation each rabbit was killed by an intravenous injection of air. At postmortem examination particular attention was paid to the testicular and lymphatic tissues, and in many cases a dark-field examination of testicular fluid was made. The tissues were not studied histologically.

RESULTS

The results of this large series of experiments with the cerebrospinal fluids of forty-two patients with various stages of syphilis were uniformly negative. The total number of rabbits studied was one hundred and fifty-seven. Seventy-seven rabbits received injections of spinal fluids (first animal passage); seventy-eight received injections of emulsions of the popliteal lymph nodes obtained from the originally inoculated animals (second animal passage), and two rabbits received injections of emulsions of the popliteal lymph nodes of two rabbits used for the second passage, representing a third animal passage. In a considerable number of instances it was thought that the testicle into which infective material had been injected had undergone slight changes, consisting chiefly of formation of small areas of thickening or induration, but in no case did the condition progress or persist. Dark-field examination of testicular fluid aspirated in these instances gave negative results.

The results of the Wassermann, Kahn and Kline tests of the blood serum of the rabbits were likewise negative. There were some examples of a "weakly positive" result, and an occasional specimen of serum was reported to show a "positive" reaction to one of the tests, but in no instance were all three tests of the same specimen positive and in none did the positive reaction persist.

COMMENT

Of the various technics employed for the demonstration of organisms in the cerebrospinal fluid of syphilitic patients, that of inoculation of rabbits has been increasingly employed (1) because by this method spirochetes have been demonstrated in fluids considered to be normal by the usual tests; (2) because it furnishes information as to the viability of the spirochetes, and (3) because it is simple. The histologic method of Warthin and Wile carried out on stained specimens of

artificially prepared spinal fluid clot and the direct method of dark-field examination of the fluid obviously give no information as to the viability of the organism. This histologic method, furthermore, requires extended experience before reliable results are assured.

By means of inoculation of rabbits viable spirochetes have been successfully demonstrated in a considerable number of fluids. As based on experiments made in the early stage of the disease, at the time of general dissemination of organisms, the results of various workers have been in general agreement. Chesney and Kemp [2] reported that spirochetes were demonstrated in five, or 14.7 per cent, of the fluids of thirty-four patients with early stages of secondary syphilis who had normal spinal fluids. As these authors pointed out, similar results were obtained in three other series of comparable cases. Thus, positive results were obtained in three, or 15 per cent, of twenty cases studied by Steiner; [3] two, or 18.8 per cent, of eleven cases reported by Arzt and Kerl,[4] and in two, or 20 per cent, of the ten cases observed by Frühwald and Zaloziecki.[5]

In later stages of the disease a number of successful results have been reported, but there are not sufficient available data to enable one to say what is the incidence of viable organisms in the fluid. There is undoubtedly great variability in individual patients, even in the case of those with involvement of the central nervous system, with respect both to the occurrence and to the persistence of organisms in the spinal fluid. In Steiner's [3] nineteen cases of neurosyphilis, the results of inoculation of rabbits were negative. Arzt and Kerl [4] reported successful results in two of six cases of dementia paralytica and in two of three cases of tabes; in two cases of cerebral syphilis the experiments were unsuccessful. In Wile's [6] eight cases, testicular inoculation of rabbits gave a high incidence of positive results; that is, spirochetes were found in the fluid in two of three cases of dementia paralytica, in one of three cases of tabes, in the one case of neurorecurrence investigated and in the one case of asymptomatic syphilis of the central nervous system. Frühwald and Zaloziecki's [5] series contained one case of a late stage of syphilis (cutaneous gumma) and three cases in which symptoms of involvement of the central nervous system were present; the single positive result was obtained in one of the cases of a later stage of the

2. Chesney, A. M., and Kemp, J. E.: Incidence of Spirochaeta Pallida in Cerebrospinal Fluid During Early Stages of Syphilis, J. A. M. A. **83**:1725 (Nov. 29) 1924.

3. Steiner, G.: Neurol. Centralbl. **33**:132, 1914.

4. Arzt, L., and Kerl, W.: Wien. klin. Wchnschr. **27**:785, 1914.

5. Frühwald, R., and Zaloziecki, A.: Berl. klin. Wchnschr. **53**:9, 1916.

6. Wile, U. J.: Am. J. Syph. **1**:84, 1917.

disease in which progressive paralysis was present. Nichols and Hough,[7] Reasoner,[8] Kemp and Chesney[9] and McIntosh and Michelson[10] were successful in demonstrating viable organisms in the cerebrospinal fluid in individual cases by inoculation of rabbits. Volk[11] also obtained a positive reaction with spinal fluid from a paralytic patient; in four other cases in which the type of disease is not mentioned, the results were negative.

Judging from these findings, it might be expected that from among the twenty-three of our patients with early stages of the disease, that is, fourteen patients with untreated early stages of syphilis (table 1), six with early stages of the disease who had received one or two treatments at least two months before the time of the observations (table 1) and three with early stages of diffuse meningitis (table 2), there would have been three or four positive results. Similarly, among four patients with neurorecurrence (table 2) not treated for from three months to five years, one positive result might have been expected. With respect to the patients with tertiary and latent syphilis negative results might probably have been predicted. The marked changes in the cerebrospinal fluid in the case of the Armenian patient with asymptomatic involvement of the nervous system may or may not have been associated with the presence of organisms.

The period of incubation of the induced infection in rabbits as reported by the aforementioned investigators was variable. As short a time as from four to seventeen days was reported by Wile, and longer periods (four months) were observed by Steiner and Volk, but in the majority of cases the period was from one and a half to three months. It should be particularly noted that in two of Chesney and Kemp's five cases in which successful results were obtained with fluids from patients with early stages of untreated secondary syphilis, positive results were not seen in the animals used for the first passage but were obtained in rabbits inoculated with emulsions of tissue from the popliteal lymph nodes and testes of the animals originally inoculated (second animals passage).

With forty of the forty-two fluids forming the basis of the present study a second animal passage was carried out. Furthermore, the period of observation was comparable to that in successful experiments reported

7. Nichols, H. J., and Hough, W. H.: Demonstration of Spirochaeta Pallida in the Cerebrospinal Fluid, J. A. M. A. **60**:108 (Jan. 11) 1913.

8. Reasoner, M. A.: Some Phases of Experimental Syphilis, J. A. M. A. **67**:1799 (Dec. 16) 1916.

9. Kemp, J. E., and Chesney, A. M.: Bull. Johns Hopkins Hosp. **36**:199, 1925.

10. McIntosh, J. A., and Michelson, I. D.: Memphis M. J. **5**:9, 1928.

11. Volk, R.: Wien. klin. Wchnschr. **26**:1824, 1913.

by other workers. The one hundred and fifty-seven rabbits inoculated were, with two exceptions, observed for more than two months, and these two animals were observed for forty-five and fifty days, respectively. The great majority, that is, one hundred and thirty-two animals, or 85 per cent, were under observation for three months or longer.

The choice of tissue from the popliteal lymph nodes for the inoculum for the second animal passage was based on the well known predilection of S. pallida for lymphoid tissue in experimental syphilis of the rabbit. The systemic infection includes involvement of the lymph nodes, and viable organisms have been recovered from the popliteal nodes in cases of latent syphilis of long standing.[12] It is theoretically possible that infection might occur without evident testicular reaction in the case of a spinal fluid containing small numbers of organisms or organisms of a low degree of virulence, but it was thought that the best chances of recovering organisms in such circumstances lay in the use of the popliteal lymph nodes.

An interesting feature of Chesney and Kemp's results, which were obtained with normal spinal fluids of patients with early stages of untreated syphilis, was that in four of their five cases in which demonstration of spirochetes was successful the patients were females. There were sixteen females and eighteen males in their series, the incidence of positive results being 25 per cent for the females and 5.5 per cent for the males. Our patients were, with five exceptions, males. Analysis of Chesney and Kemp's results by the chi-square test of homogeneity,[13] however, shows that the difference in incidence of their positive results between the two sexes is not statistically significant (chi-square = 2.406; $p = 0.01$). That is, the chances of obtaining a positive result were not better with the spinal fluids of their female patients than with those of their male patients.

There are three features in which our material differs from that of others who have been successful in demonstrating spirochetes in the spinal fluid of syphilitic patients. The first concerns the organism involved. As far as is known—and it is certainly reasonable to presume that such was the case—the infection in all our patients could be attributed to an organism of Oriental source. The question whether such strains differ in their biologic characteristics from strains obtained from Occidental sources was investigated in a series of experiments on rabbits carried out in Peiping and in New York.[14] The results of this work

12. Pearce, L., and Brown, W. H.: J. Exper. Med. **35**:39, 1922.

13. Fisher, R. A.: Statistical Methods for Research Workers, London, Oliver & Boyd, 1930.

14. Pearce, L.: Unpublished data.

indicate that as far as the reaction of the rabbit was concerned, the essential pathogenic properties of the Oriental and those of the Occidental strains which were studied were similar.

The second difference is that our inoculations were made in native albino rabbits obtained in Peiping while those of other workers were made in American and European rabbits. It is known that breed may have a definite influence on the course of experimental syphilis in the rabbit,[15] and extensive experience with a rabbit-breeding colony has shown that the factor of breed is significantly associated with the host's reaction to a variety of conditions. In the present instance, however, it does not appear probable that the use of Chinese rabbits could be the sole reason for the uniformly negative results obtained. The comparative experiments just referred to included the use of both Chinese and American rabbits, and in every instance intratesticular inoculation induced a well marked orchitis. In certain respects the pathologic picture appeared to be influenced by the particular breed of animal used, but the findings did not suggest such a level of insusceptibility or resistance as to bring about completely negative results.

The third difference is that of race, the majority of our patients being Chinese while those of other workers were white persons or Negroes observed in Europe and America. So far as the clinical manifestations were concerned, those observed in our patients did not differ from those exhibited by patients in the Occident. The opinion has been expressed, however, that syphilis in the Orient differs from that in the Occident chiefly with respect to a lower incidence of involvement of the central nervous system. Physicians with extensive clinical experience in Oriental countries report comparatively few cases of locomotor ataxia or dementia paralytica in native patients, in contrast to the expected incidence of such conditions in their white patients. Furthermore, the reaction to syphilis of Negroes differs in many respects from that of white patients, as has been shown by several observers, notably by those at the Johns Hopkins Hospital.[16] That Chinese patients may also present peculiarities or differences of reaction is entirely possible, and the results of this study may be an instance in point.

It is known that the presence of viable organisms is not necessarily associated with cellular and other abnormalities of the fluid, while the recovery of organisms from abnormal fluids appears to be unpredictable. In the light of the uniformly negative results obtained on a mixed series of forty patients with a technic which gave ample opportunity for the recovery of viable organisms, it appears either that the true incidence of viable S. pallida in the spinal fluids of syphilitic patients is not as

15. Rosahn, P. D.: J. Exper. Med. **57**:907, 1933.
16. Turner, T. B.: Bull. Johns Hopkins Hosp. **46**:159, 1930.

high as has been thought or that the reaction of Chinese patients to S. pallida is of such an order that viable organisms either find their way less frequently into the cerebrospinal fluid or do not persist there as long as appears to be the case in patients of other races. Perhaps both explanations are applicable. Until the results in other series are available, however, the present observations may be tentatively interpreted on the basis of differences or peculiarities in the racial character of the reaction to syphilitic infection.

CONCLUSION

The attempt to demonstrate S. pallida in the cerebrospinal fluids of forty Chinese and two European syphilitic patients by means of inoculation of rabbits was uniformly unsuccessful.

EVALUATION OF THE PHYTOPHARMACOLOGIC TEST OF PELS AND MACHT

FURTHER REPORT

LESTER HOLLANDER, M.D.
AND
RAYMOND J. GREB, PH.D.
PITTSBURGH

The phytopharmacologic test devised by Pels and Macht [1] for determining the toxicity of the blood serums of patients with anemia and various diseases has been applied by us. In some cases modifications of the tests were attempted. A summary of this work is reported.

The technic of the test has already been published several times by the originators. It consists in measuring the amount of retardation of the growth of rootlets in a plant nutrient solution to which has been added a small percentage of a patient's blood serum. The modifications used in our laboratory are as follows:

1. Not only a solution containing 1 per cent but also solutions containing 5, 10, 25 and 33 per cent serum were used.

2. It was found [2] that seedlings of Zea mays (popcorn) responded similarly to those of Lupinus when exposed to a test solution. Other plants used in these tests were Raphanus (radish), Fagopyrum (buckwheat), Allium (onion) and Salix (swamp-willow cuttings with sprouted rootlets).[3]

3. In addition to the tests consisting of the first twenty-four hour immersion in a plant nutrient solution containing serum (reading A) measurements were made after a second twenty-four hour period of growth of the same seedlings in a normal plant nutrient (Shive) [4] solution (reading B).

From the Pittsburgh Skin and Cancer Foundation.

1. Pels, I. R., and Macht, D. I.: Phytopharmacology of Pemphigus and Other Dermatoses: Additional Studies, Arch. Dermat. & Syph. **23**:601 (April) 1931.

2. Hollander, Lester, and Greb, Raymond J.: Evaluation of the Phytopharmacologic Test of Pels and Macht, Arch. Dermat. & Syph. **33**: 1012 (June) 1936.

3. Greb, Raymond J.: Various Plants in the Phytopharmacological Test, Proc. Pennsylvania Acad. Sc. **9**:98, 1935.

4. Shive, J. H.: A Study of Physiological Balance in Nutrient Media, Physiol. Researches **1**:327, 1915.

PRESENTATION OF DATA

The data presented here have been summarized and grouped in the following manner: (*a*) according to diseases, (*b*) according to plants used, (*c*) according to the percentage of serum in the nutrient solution (test solution) and (*d*) according to sex when enough similar tests were made to permit grouping in this manner. No summaries according to age were attempted since it was obvious that extreme variation occurs regardless of age, and, moreover, the ages of the persons tested were too distantly separated to permit grouping.

Syphilis.—Serums from thirty-one patients receiving antisyphilitic treatments were tested. The averages recorded were extremely variable in the different cases. Results from eighteen serums tested with Raphanus in a solution containing 5 per cent serum ranged from a low average of 0.58 mm. to a high of 4.68 mm. for reading A. The grand average of growth established for this group from the aforementioned eighteen serums was 2.95 mm. The average number of plants used in each test was 18. The ten serums tested with Lupinus under similar conditions gave a grand average of 3.31 mm., 27 plants being the average number used in each test reading A (table 1). Plants used in the aforementioned ten tests when measured after the second immersion (reading B) gave a grand average of 6.93 mm.

A few tests were made with Zea mays and Fagopyrum, but the data are too limited for presentation.

When the foregoing data were grouped according to sex, thirteen tests with Raphanus made on serums from male patients showed an average growth of 3.37 mm. and five tests on serums from female patients gave an average growth of 1.90 mm. With Lupinus, tests of six serums from males gave an average reading of 2.99 mm., and those of four serums from females gave an average of 3.99 mm.

Pemphigus.—Thirteen tests were made on the serums of six patients with pemphigus. Five tests were made with Lupinus in a solution containing 5 per cent serum. The grand average for serums from patients with pemphigus (reading A) was 3.84 mm., 31 seedings for each test. Four of the groups of test plants measured after the second immersion (reading B) showed an average growth of 9.39 mm.

The grand average for the four tests with solution containing 1 per cent serum was 7.75 mm., an average of 39 seedlings being used for each test. When three of these four test plants were exposed to the second immersion (reading B) the average growth was 10.79 mm.

Seedlings of Zea mays in a solution containing 1 per cent serum gave a grand average of 4.73 mm. for six tests (reading A). The average number of seedlings used for each test was 53. Four of these seedlings when exposed to the second immersion (reading B) showed a grand average of 10.68 mm.

Records of other tests with Zea mays in solution containing 5 per cent serum as well as with other plants in various solutions are too meager to consider here.

The average results of tests on the serum from one female patient (case 163) with Lupinus in a solution containing 1 per cent serum ranged from 13.27 to 5.62 mm. after forty days. This patient was receiving treatment for active pemphigus. About eighty days later, a solution containing 1 per cent of her serum elicited a

TABLE 1.—*Summary of Averages with Lupinus as the Test Plant*

Condition of Patient	1 per Cent Solution Reading A, Grand Average, Mm.	Number of Serums Tested	Average Number of Plants Used	Lowest Average, Mm.	Highest Average, Mm.	Reading B, Grand Average, Mm.	Number of Serums Tested	Lowest Average, Mm.	Highest Average, Mm.	5 per Cent Solution Reading A, Grand Average, Mm.	Number of Serums Tested	Average Number of Plants Used	Lowest Average, Mm.	Highest Average, Mm.	Reading B, Grand Average, Mm.	Number of Serums Tested	Lowest Average, Mm.	Highest Average, Mm.
Syphilis	4.70	2	20	3.40	6.00	7.43	2	6.60	8.27	3.31	10	27	1.91	7.05	6.93	9	2.50	11.86
Pemphigus	7.75	4	39	5.62	13.27	10.79	3	9.43	13.30	3.84	5	31	2.50	9.25	9.39	4	6.34	12.26
Pernicious anemia	5.75	10	48	3.35	7.84	9.47	9	6.21	11.60	2.14	7	24	0.45	4.71	7.15	7	3.97	10.70
Miscellaneous dermatitis	6.56	8	61	3.10	10.70	8.85	8	5.54	12.92	3.49	8	22	1.35	5.73	9.22	7	6.20	12.92
Cancer of breast	....	..	..	....	.....	.....	..	....	.....	3.56	7	18	2.40	5.40	6.70	7	2.61	9.16
Cancer of lip	....	..	..	....	.....	.....	..	....	.....	3.58	6	19	2.71	5.37	8.39	6	7.30	9.21
Cancer of cervix	....	..	..	....	.....	.....	..	....	.....	3.45	5	20	2.02	5.70	7.75	5	6.80	8.88
Lymphosarcoma	....	..	..	....	.....	.....	..	....	.....	3.66	4	21	2.88	4.55	7.09	4	6.07	8.61
Miscellaneous cancers	7.12	4	50	4.84	9.41	9.97	3	7.27	12.73	3.42	10	20	1.05	5.94	6.87	10	4.05	9.88
Normal	6.54	7	45	4.52	11.24	.....	..	....	.....	3.10	22	17	0.85	5.20	7.25	18	4.58	10.72

TABLE 2.—*Summary of Averages with Zea Mays as the Test Plant*

Condition of Patient	1 per Cent Solution Reading A, Grand Average, Mm.	Number of Serums Tested	Average Number of Plants Used	Lowest Average, Mm.	Highest Average, Mm.	Reading B, Grand Average, Mm.	Number of Serums Tested	Lowest Average, Mm.	Highest Average, Mm.	5 per Cent Solution Reading A, Grand Average, Mm.	Number of Serums Tested	Average Number of Plants Used	Lowest Average, Mm.	Highest Average, Mm.	Reading B, Grand Average, Mm.	Number of Serums Tested	Lowest Average, Mm.	Highest Average, Mm.
Syphilis	5.50	1	20	....	.....	6.55	1	....	.....	3.34	2	22	3.16	3.34	....	..	....	.....
Pemphigus	4.73	6	53	1.91	7.42	10.68	4	8.80	11.50	3.60	3	19	2.30	5.33	8.99	3	6.80	11.11
Pernicious anemia	4.21	8	47	1.37	5.12	9.32	8	8.34	10.45	2.06	5	19	1.15	3.55	10.16	19	8.38	11.36
Miscellaneous dermatitis	5.05	3	24	4.06	6.15	8.46	3	7.48	10.10	2.26	3	14	1.50	3.54	10.40	3	8.54	12.38
Cancer of breast	....	..	..	....	.....	.....	..	....	.....	3.19	6	18	1.44	4.32	5.94	6	2.60	7.35
Cancer of lip	....	..	..	....	.....	.....	..	....	.....	3.50	5	24	2.45	5.10	7.99	5	5.61	11.37
Cancer of cervix	....	..	..	....	.....	.....	..	....	.....	4.06	2	16	2.62	5.51	7.68	2	7.00	8.37
Lymphosarcoma	....	..	..	....	.....	.....	..	....	.....	....	..	..	....	....	....	..	....	.....
Miscellaneous cancers	5.64	3	40	4.55	6.20	9.26	2	8.83	9.60	3.14	8	21	0.61	4.59	6.40	8	2.93	10.63
Normal	4.15	4	26	2.90	6.50	7.04	2	6.02	8.06	3.57	7	32	0.90	6.47	10.70	6	6.59	13.86

growth of 6.32 mm. Recently serum from one male patient (case 200) presenting an advanced stage of treated pemphigus gave a reading of 5.81 mm. (reading A) with Lupinus in solution containing 1 per cent serum.

Anemia and Leukemia.—There were seventeen tests with blood serums from fifteen patients having some form of pernicious anemia, secondary anemia or lymphatic leukemia. In most of these tests both Lupinus and Zea mays as well as various concentrations of the serums were used.

Ten serums tested with Lupinus in solution containing 1 per cent serum produced an average of 5.75 mm. (reading A). The average number of seedlings used in each test was 48 (table 1). In the second series of tests nine of these ten serums produced an average of 9.47 mm. (reading B).

Reading A on Lupinus in a solution containing 5 per cent serum (table 1) showed an average growth of 2.14 mm. for seven serums tested, an average of 24 seedlings per test being used. Reading B on plants tested with the seven serums averaged 7.15 mm.

Eight serums tested with Zea mays (table 2) in a solution containing 1 per cent serum showed an average growth of 4.21 mm. Forty-seven seedlings were used in each test on the average. Reading B on plants tested with these serums showed an average growth of 9.12 mm.

An average of 2.06 mm. (reading A) was established for five serums with Zea mays (table 2) in solution containing 5 per cent serum. The average number of seedlings used in these tests was 19. Reading B showed 10.16 mm. as a grand average.

Reading A on plants tested with solution containing 1 per cent serum, the serums being grouped according to the patient's sex, showed the following results: With Lupinus four tests on serums from male patients showed an average growth of 5.79 mm.; six tests on serums from female patients gave an average growth of 5.74 mm. With Zea mays six tests on serums from females showed an average growth of 4.17 mm., and an average growth of 4.31 mm. was obtained from two tests on serums from males. Readings for the solution containing 5 per cent serum were similarly variable.

Miscellaneous Dermatoses.—Under this heading are grouped such disorders as pruritus, epidermolysis, erythema, acne and scabies. The same degree of variation was noted between results of tests on serums from patients with these diseases as between those of tests on serums from anemic, syphilitic and normal persons. Eight serums tested with Lupinus in solution containing 1 per cent serum (table 1) elicited the following readings: reading A, grand average, 6.56 mm., 61 seedlings in each test; reading B, grand average, 8.85 mm. Eight serums tested in solution containing 5 per cent serum gave the following results: reading A, grand average 3.49 mm. (average number of seedlings, 22); reading B, grand average 9.22 mm.

Only three serums were tested with Zea mays in solution containing 1 per cent serum. The following averages were obtained: reading A, grand average, 5.05 mm. (24 seedlings); reading B, grand average 8.46 mm. Three serums tested by means of solution containing 5 per cent serum gave results as follows: reading A, grand average 2.26 mm (14 seedlings); reading B, grand average 10.40 mm.

Malignant Conditions.—Serums from fifty-two patients with carcinoma of various organs were tested. This series comprised (*a*) ten patients with carcinoma of the breast, (*b*) eight with carcinoma of the lip, (*c*) eight with carcinoma of the cervix, (*d*) five with lymphosarcoma and (*e*) twenty-one with carcinoma involving some part of the body other than those listed.

Serums from seven of the patients with carcinoma of the breast were tested with Lupinus in solution containing 5 per cent serum (table 1). An average growth of 3.56 mm. (reading A) was obtained. Eighteen seedlings on the average were used in each test. Reading B showed a grand average of 6.7 mm.

Six tests with Zea mays (table 2) in solution containing 5 per cent serum showed an average growth of 3.19 mm., an average of 18 seedlings being used in each test. Reading B for this group averaged 5.94 mm.

Serums from patients with carcinoma of the lip gave about the same results. Six serums were tested with Lupinus (table 1) in solution containing 5 per cent serum. These gave an average of 3.58 mm. (reading A) with 18 plants for each test. Reading B showed an average of 8.39 mm.

Zea mays in solution containing 5 per cent serum (table 2) showed an average growth of 3.50 mm. in five tests, 24 plants being used for each test; reading B showed an average growth of 7.99 mm.

Readings obtained for the patients with other types of tumors showed similar variation. Average readings are listed in tables 1 and 2.

Observations on Serum from "Normal" Persons.—A summary of the tests in which serums from "normal" persons (persons with no demonstrable disease) were used shows the following averages: Twenty-two serums tested with Lupinus in solution containing 5 per cent serum (table 1) gave an average reading of 3.10 mm. of growth with an average of 17 seedlings per test. Reading B on eighteen tests showed an average of 7.25 mm.

Seven serums were tested by means of solutions containing 1 per cent serum. The average obtained from these was 6.54 mm., Lupinus being used. The average number of seedlings was 45.

With Zea mays (table 2) the following averages were obtained in solutions containing 5 per cent serum: Reading A, grand average for seven serums 3.57 mm. (average number of seedlings, 32); reading B, grand average 10.70 for six tests.

Plant Nutrient Solutions Only.—Lupinus grown in the plant nutrient solution gave an average of only 9.79 mm. for the 586 plants tested. This figure may be used as the basis for comparison in estimating the phytotoxic index of any one serum. Zea mays grown under the same conditions showed an average growth of 9.86 mm. for the 317 plants tested.

COMMENT

From the data now available in this laboratory it seems obvious that the encouraging results obtained by Macht and his co-workers in their work on pernicious anemia and pemphigus vulgaris were not duplicated here.

While it may be maintained that the data here presented do show a low phytotoxic index in some cases of both pernicious anemia and pemphigus vulgaris, there are also many nonconformist cases. An index of over 130 in a case of suspected, and later proved, pemphigus (case 163) indicates that the test is unreliable. The extremely low indexes that are most difficult to explain on the basis of specific toxicity, however, are those obtained from the tests on serums from "normal" persons as well as on those from patients with conditions listed under

carcinoma, syphilis, etc. In all the latter groups the readings should be above any obtained with serums from patients with pemphigus or anemia, according to the evidence presented by Macht and his co-workers. In the data shown in tables 1 and 2, indexes as low as any obtained with serums from patients with either anemia or pemphigus may be noted.

The variations observed when the plants were immersed for a second twenty-four hour period in a plant nutrient solution to which no serum had been added further substantiate the weakness of the phytopharmacologic tests. All the plants immersed in a solution containing serum showed a subsequent effect when observed for a second twenty-four hour period. No uniform result was obtained during this period after any of the tests on serums, as recorded in table 1. The same incongruous variations are shown in table 2. In some instances, when the retardation of growth was great during the first twenty-four hour period, the amount of growth obtained during the second twenty-four hour period was also low. Many exceptions may be noted from table 1.

SUMMARY AND CONCLUSIONS

No uniformity of growth could be obtained with any of the series of serums from patients with the diseases tested.

The readings obtained for serums from patients with pernicious anemia or pemphigus vulgaris show variations as low as do readings for serums from patients with carcinoma or syphilis or for serums from normal persons.

Many of the variable results obtained may be ascribed to differences in individual growth potentials of seedlings.

A genetically homozygous strain of plant rootlets must be developed. This would reduce growth potential differences.

As was previously pointed out,[2] in order to get a reliable measure of toxicity the number of plants exposed to a test must be great enough to insure a statistically sound mean of growth. Such a test becomes a real time-consuming problem, and since, at best, the test seems to be of doubtful value as a diagnostic measure, some modification of the technic, such as producing a strain of seedlings genetically uniform in their root growth potential,[3] must be developed.

XERODERMA PIGMENTOSUM

AN INHERITED DISEASE DUE TO RECESSIVE DETERMINERS

MADGE THURLOW MACKLIN, M.D.
LONDON, CANADA

Despite the rapid growth of genetics in the last quarter of a century, there is little in the modern medical textbooks to indicate the applications of genetics to medicine. Statements that are obviously incorrect with respect to the inheritance of disease still find a place in modern textbooks. To some extent this is true of the rare condition of xeroderma pigmentosum. Although it was early recognized that this disease is in part dependent on a constitutional factor, it is not generally conceded that this factor is inherited. Thus, one still finds the statement that xeroderma pigmentosum is not hereditary but "familial." In the 1927 edition of his textbook on diseases of the skin Sequeira stated: "It does not appear to be hereditary, the fact that the patients rarely survive puberty probably explaining this." This mistaken idea is due, as will shortly be seen, to a misunderstanding of what is meant by the term hereditary.

There are other erroneous statements in the literature on this disease, and, as will be shown later, they are all made because of inadequate understanding of the operation of the laws of inheritance. Thus, although it is not generally conceded that xeroderma pigmentosum is hereditary, the statement is frequently encountered that more than one child in the family is usually affected. Hence, the disease is called familial. I shall point out that the disease is hereditary but that, in spite of this, because of the nature of its transmission, only one child is affected in the majority of families. This statement may sound paradoxical, but it is easily comprehended when the laws of inheritance are understood.

Another mistaken idea is that, although in the aggregate males and females are equally affected, only one sex is involved in any one family —that is, one family has only sons affected and another only daughters, but as a rule both sexes are not affected in the same family. If the disease is hereditary this statement at once is called into question, for there is no known mechanism in heredity which permits such a peculiar distribution of the disease. If such a distribution occurs between the sexes, it must be accepted, and one must admit that there is no key

From the University of Western Ontario Medical School.

to the explanation. It becomes imperative, therefore, that the data be examined to see whether the statement is founded on fact.

A third statement which one encounters is that not only does this disease tend to affect one sex in any given family but it tends to affect all the members of that sex in the family. If the disease is inherited, one is at a loss to explain this statement, for again there is no known mechanism by which such a result could be accomplished.

The present paper attempts to prove the following assertions: 1. Xeroderma pigmentosum is inherited, and the term familial is a misnomer not only for this but for any disease and should be dropped. 2. Xeroderma pigmentosum is dependent on a set of recessive determiners located in a pair of chromosomes not connected with sex. The method of proof here depends not on experimental matings but on the application of mathematical formulas. It will be shown that the observed data on xeroderma pigmentosum agree with the expectations demanded by the formulas on theoretical grounds. The incidence of cousin marriages among the parents of the patients will be used as further proof of the mode of transmission of this inherited disease. 3. The disease tends to affect not more than one child in the majority of families, although the occurrence of two or more affected children in one family is not rare. 4. It does not tend to affect one sex only in a family but may affect the two sexes equally. 5. Not all the members of one sex tend to be affected in any family, this involvement being the rare rather than the usual occurrence. These misconceptions should disappear from the literature on xeroderma pigmentosum.

IS XERODERMA PIGMENTOSUM INHERITED?

It is necessary first to examine the data on which rests the idea that this disease is not inherited. This belief had its foundation in the old misconception of what is meant by hereditary. Formerly it was thought that for a condition to be called inherited it had to be present in parent and child, generation after generation. When a trait or character suddenly appeared in one or more children of a family, with no previous history of it in the ancestors, it was said to be familial but not hereditary. In practically all cases xeroderma pigmentosum appears in children whose parents and ancestors were not similarly affected. Hence, xeroderma pigmentosum was said to be not hereditary but familial.

Today, of course, this conception has changed, owing to the work of the experimental geneticist, who has shown that in lower forms the so-called familial conditions are just as hereditary as those which descend from generation to generation as obvious characters. They differ from conditions of the latter type, however, in this way: They require a double dose of the determiner before the condition can become obvious.

Two parents both of whom carry but one determiner for the condition and hence do not show the character may produce obviously affected offspring, since each may pass on his or her single determiner to the child. The child thus receives a double quantity, and the character develops as an obvious one. Such characters are said to be due to recessive determiners, in contrast to the characters which are passed on from parent to child, generation after generation, and are said to be due to dominant determiners. But in either case the character is inherited, for it is determined by forces which reside in the germ cells, which are the sole connecting link between parent and child. The term familial in contrast to hereditary should be dropped from medical literature, as it perpetuates a conception which genetics has shown to be erroneous. Therefore, the fact that the parents of patients with xeroderma pigmentosum are themselves unaffected by the disease in no way militates against the conception that this disease is an inherited one, due to factors which are present in the germ cells. It is merely understood that the disease does not behave as though it were dependent on dominant factors. The fact that it tends to be concentrated in a few families, however, leads one to the hypothesis that it may be dependent on recessive determiners.

IS XERODERMA PIGMENTOSUM INHERITED AS A RECESSIVE CHARACTER?

That this disease is inherited and is dependent on recessive factors cannot be proved by the method used by the experimental geneticist—by appropriate matings—but certain mathematical formulas can be applied to the observations which have been deduced from the recognized behavior of conditions proved to be recessive in their mode of inheritance. If these mathematical formulas agree with the observed data, one may conclude that the hypothesis is workable. The more criteria one has by which to test the observed data the stronger will be the proof that the hypothesis is correct, provided, of course, that the data are in agreement with the criteria. To apply these formulas, there must be a large number of cases, and so it is necessary to collect and analyze as many of the reported cases of xeroderma pigmentosum as possible. It is true that the question of the accuracy of diagnosis enters here, but this need not trouble one too much. The characteristics of this disease are rather clearcut, and there is little that is likely to confuse the picture. If there was any question as to the accuracy of the diagnosis the case was omitted from the series reported in this paper.

Although reports of about 460 cases of xeroderma pigmentosum have appeared in the literature, some of these were published in foreign journals which were inaccessible to me. The available accepted cases numbered 170. Since there is no reason to suppose that the cases

TABLE 1.—*Data on 198 Families in Which Xeroderma Pigmentosum Appeared*

A. Families with Complete Family History

Author	No. of Children Affected in Family			No. of Normal Children in Family			Parents Related	Comment
	Male	Female	Sex Not Stated	Male	Female	Sex Not Stated		
Adrian	1	..	..	1	..	..	First cousins	Jewish
Anderson	1	1	..		None		.....	
Andrews	..	1	..		None		.....	
*Archambault	2	1	..	2	..	..	.....	
*Bandler	1	2	..	..	..	9	.....	
Becker, Pautrier and Woringer	1	..	..	1	5	..	First cousins	2 children died in infancy
*Bernoulli	2	2	..	..	..	5	.....	
Bowen	1	..	..	..	..	4	.....	
*Brault	..	1	..	1	..	..	.....	
Brayton	1	2	..	3	..	1	Not related	
Cannon	..	2	1	..	..	3	Not related	Italian
Canright	1	..	..	5	2	..	.....	Five boys and 1 girl died in infancy; paternal grandfather said to have been affected
*Cedercreutz	1	2	..	..	..	4	Not related	Italian
Cedercreutz	1	1	..	..	..	4	Not related	Italian
Cedercreutz	1	1	..	..	..	8	Not related	Italian
Cole and Driver	..	1	..	1	1	..	First cousins	
Copeland and Martin	..	1	..	1	2	..	First cousins	Jewish
Copeland and Martin	..	3	..	..	3	..	Not related	
Copeland and Martin	..	1	..		None		Not related	
Corlett	1	..	..		None		First cousins	1 miscarriage at 3 mo.
Corson and Knowles	2	1	..	1	2	..	First cousins	2 girls died in infancy
Crocker	1	2	..	..	1	..	.....	
*Crocker	1	1	..	..	1	..	.....	
*Danlos	1	1	..	1	3	..	.....	
Dennie	2	1	..	1	1	..	.....	
*Dörffel	..	2	..	..	..	6	Related	European stock
Duhring	..	1	..	3	1	4	.....	Four children of unknown sex died in infancy
*Eliassow	2	1	..	..	..	5	Not related	
*Engmann	1	1	..	1	..	..	.....	
Fox	2	..	..	2	..	..	First cousins	
*Freund	..	2	..	..	..	12	First cousins	
*Fuss	..	1	..	..	1	..	First cousins	
*Geber	..	2	..	1	..	..	.....	
*Greeff	2	..	..	2	2	..	.....	
Grindon	1	1	..	2	..	..	.....	Mother freckled heavily
*Hahn and Weik	..	2	..	..	6	..	.....	
Halle	..	1	..	..	..	2	.....	
Hayman	1	..	..	1	..	..	Not related	
Herxheimer	1	1	..	..	..	4	.....	
Hunter	3	..	..	1	4	..	.....	1 child died at age of 2½ years
Hutchins	1	..	..	..	1	..	First cousins	
*Hyde	1	2	..	3	..	2	.....	
Jeanselme and Hufnagel	1	..	..	..	..	1	Second cousins	
*Junès	1	..	..	1	1	1	First cousins	Arab
Junès	1	1	..	..	..	2	First cousins	Arab
Kaposi	..	2	..	..	..	2	.....	
Kaposi	..	1	..	2	6	..	.....	
Kerl	..	1	..	..	..	7	.....	
Kessler	1	2	..	1	2	1	Not related	
*Klein	4	..	..	3	2	..	Second cousins	
Klein	..	..	1	..	..	..	.....	Child of 1 of the normal sisters of the preceding family
Kren	..	1	..	..	..	3	.....	
Kring	1	..	..		None		.....	2 half-brothers normal
*Kudish	2	1	..	2	4	..	.....	
Kudish	..	2	..	..	1	2	.....	
Lane	..	1	..	..	4	..	Second cousins	
*Lederer	1	1	..	2	..	..	.....	
*Lenz	..	..	3	..	..	6	.....	
*Lesser and Bruhns	..	2	..	..	1	..	.....	
*Leszczyński	2	..	..	1	7	..	Related	

TABLE 1.—*Data on 198 Families in Which Xeroderma Pigmentosum Appeared —Continued*

A. Families with Complete Family History—Continued

Author	No. of Children Affected in Family			No. of Normal Children in Family			Parents Related	Comment
	Male	Female	Sex Not Stated	Male	Female	Sex Not Stated		
Lord	1	..	..	..	1	..	First cousins once removed	
*Lukasiewicz	2	..	..	..	1	..	.....	
Lukasiewicz	1	..	..	2	1	..	.....	This family and the next family reported by this author were related
Lukasiewicz	..	..	1	..	..	..	.....	
Lynch	..	1	..	..	..	7	Not related	
*Mendes da Costa	1	1	..	1	1	..	.....	
*Metscherski	2	1	..	..	..	3	.....	
*Metzenauer	1	1	..	3	5	..	.....	
*Migliorni	..	3	..	2	1	..	.....	
Montgomery	..	1	..	3	1	..	Not related	2 boys died in infancy
*Monthus	..	1	..		None		.....	This child was first cousin of the two in the second family reported by Monthus
Monthus	..	2	..	2	..	..	First cousins	
Murphy	1	1	..	..	..	5	.....	
*Nemeth	1	..	..	..	..	2	Second cousins	
Nicolas, Favre and Dupasquier	1	1	..	2	1	..	.....	
*Nicolas, Favre and Dupasquier	..	2	..	2	..	4	.....	
*Nicolle	..	1	..	4	2	..	.....	Italian
Nicolle	1	..	..	2	1	..	.....	Tunisian
Nicolle	1	..	..	1	1	..	.....	
Nicolle	1	..	..	..	4	..	.....	French
Nicolle	3	..	..	3	1	..	.....	Tunisian
Nicolle	1	1	..	..	1	..	.....	
*Okamura	1	1	..	..	3	..	.....	
Oulmann	2	..	..		None		.....	Parents German and Irish
*Per	1	..	..		None		First cousins	Jewish
Pernet	..	1	..		None		Not related	
Phillips	..	1	..	..	2	..	First cousins	
Pick	1	2	..	..	..	9	.....	Cited by Taylor
*Piéchaud	2	..	..		None		.....	
Potter	..	1	..	..		..	.....	
Quinquand	..	2	..	1	..	..	.....	
*Raynaud	2	..	..	3	4	..	.....	These children were half-brothers of the affected girl in the second family reported by Raynaud
Raynaud	..	1	..		None		.....	
Rich	2	..	..	..	..	6	.....	
Rouvière	..	3	..	4	1	..	Second cousins	Cited by Ormsby
Ruder	7	..	..	1	5	..	Second cousins	Cited by Councilman
*Scherber	2	..	..	3	..	..	Second cousins	
Simpson	1	1	..	9	5	..	First cousins	4 normal children died
Simpson	..	1	..	..	..Several†		Second cousins	
*Stein	..	2	..	2	..	..	.....	
Steinberg	2	..	..	..	1	..	.....	The 2 children affected were brothers of the mother of the 2 affected boys in the second family reported by Steinberg
Steinberg	2	..	..	..	..	2	.....	
Stout	1	..	1	..	..	2	.....	
Taylor	1	1	..	2	2	..	Second cousins	Jews; the mother of this group and the mother of the second group reported by Taylor were sisters
Taylor	..	3	..	..	..	7	First cousins	
Taylor	..	1	..	..	..	5	.....	Jews
Taylor	..	1	..		None		.....	Jews
*Tenneson	1	1	..	1	1	..	.....	
*Teterjanz	..	3	..	1	1	..	.....	These two families reported by Teterjanz were related

TABLE 1.—*Data on 198 Families in Which Xeroderma Pigmentosum Appeared —Continued*

A. Families with Complete Family History—Continued

Author	No. of Children Affected in Family			No. of Normal Children in Family			Parents Related	Comment
	Male	Female	Sex Not Stated	Male	Female	Sex Not Stated		
Teterjanz	..	2	..	2	..	..	.....	
*Thibierge	1	..	..	1	..	..	First cousins	These 2 affected children were also first cousins
Thibierge	..	1	..	4	2	..	First cousins	
*Unna	..	..	2	..	..	4	.....	
Vidal	..	1	..	2	..	..	.....	Cited by Taylor
Vidal	1	..	..	1	1	..	.....	
Vidal	1	..	..	3	1	..	.....	
*Vidal	3	..	..	1	1	..	.....	
*Vidal	..	2	..	2	..	..	.....	
Walker	..	3	..	None			.....	The half-sister by their father's first marriage and the half-sister by their mother's second marriage were normal
White	2	..	..	2	3	..	.....	Russian Jews
White	..	1	..	Several‡			Not related	
*White	2	..	..	2	2	..	.....	
Whittle	..	1	..	None			First cousins	
Withers	1	..	..	1	1	..	.....	
De Wolf	..	1	..	..	..	3	Not related	
von Zumbusch	1	..	..	..	2	..	.....	Several sisters were said to be normal, which I have stated as 2
von Zumbusch	..	3	..	1	..	5	Distant relatives	

B. Families with Incomplete Family Histories

Author	Number of Children Affected in Family			Parents Related	Comments
	Male	Female	Sex Not Stated		
Adams	..	..	1	.....	
Alderson	..	1	..	Related	
de Amicis	1	1	..	Not related	
*Arnozan	3	..	..	.....	
*Artom	2	..	..	.....	
*Beron	..	2	..	.....	
Blackman	1	1	..	.....	
Chance	1	..	1	First cousins	Jewish
Corlett	1	..	..	.....	Father also said to have been affected
Councilman and others	..	2	..	.....	
*Diaz	1	1	..	Second cousins	
*Dies	1	1	..	.....	
Dobell	1	..	..	.....	1 sister freckled easily
Dubois-Havernith	1	..	..	.....	Cited by Taylor
Eller	1	..	..	.....	Jewish
Fox	1	..	..	.....	
Fuchs	..	2	..	.....	Cited by Nelson
Freeman	1	1	..	.....	
*Funk	..	2	..	.....	
Gottheil	1	..	..	.....	
Grier	1	1	..	.....†	The woman in the second family was paternal aunt to the two in the first, the aunt's father and great-grandfather were said to have been affected
Grier	..	1	..	.....	
Guy and Jacob	..	1	..	Not related	
Heitzmann	1	..	..	.....	Cited by Taylor
Herxheimer	1	1	..	.....	
*Jamieson	..	2	..	.....	
*Junès	1	1	..	.....	Tunisian
Kaposi	..	1	..	.....	
Kaposi	1	1	..	.....	Italian
Kaposi	..	1	..	.....	
Kaposi	1	..	..	.....	
Kaposi	1	..	..	.....	
*Kiewer	2	1	..	.....	

TABLE 1.—*Data on 198 Families in Which Xeroderma Pigmentosum Appeared —Continued*

B. Families with Incomplete Family Histories—Continued

Author	Number of Children Affected in Family: Male	Female	Sex Not Stated	Parents Related	Comments
*Kreibich	1	1	..	First cousins	
Kren	2	..	..	.....	
Lane	1	..	..	.....	
Lane	..	1	..	.....	
*Loeb	1	1	..	Not related	
Louste, Callian and Ducourtioux	..	1	..	.....	Jewish
*Löw	2	..	..	.....	
*Lustgarten	1	1	..	.....	
Markowitz	..	1	..	.....	
*Moberg	3	3	..	.....	
*Morini	1	1	..	First cousins	
*Mukai	1	..	..	Related	Japanese
Neisser	2	..	..	.....	Cited by Taylor
Nelson	..	..	1	.....	
*Nicolle	2	..	1	.....	Tunisian
*Nobili	1	..	1	.....	
*Ohmichi	1	..	2	First cousins	Japanese
*Perls	..	2	..	.....	
*Peyri	..	2	..	.....	
*Reines	..	2	..	.....	
*Rotch	..	2	..	.....	
Sachs	..	1	..	.....	
Schamberg	2	..	..	First cousins	
de Sanctis	2	1	..	.....	
Seale	1	1	..	.....	
*Segawa	1	2	..	.....	Japanese
Simpson	1	..	..	.....	
*Stein	2	2	..	.....	
*Toyama	1	..	3	.....	Japanese
Toyama	..	2	..	.....	Japanese
Vidal	..	1	..	.....	Cited by Taylor
Vidal	1	..	..	.....	
Vignolo-Litati	..	1	..	First cousins	
*Volk	1	1	..	.....	
Way	1	..	..	.....	Greek
Williams	..	1	..	.....	
von Zumbusch	..	1	..	.....	
Total	167	175	19		

* The asterisk indicates the cases which were cited by E. A. Cockayne.
† Two of these children were listed as normal in table 2.
‡ Three of these children were listed as normal in table 2.

reported in the journals to which I had access were different from those the records of which were not reviewed, it is probable that the conclusions drawn from these 170 cases would not be appreciably altered if the entire series of cases were available. Since the analysis of these 170 cases was completed I have had access to the recently published work of Cockayne. In this study he listed many of the case reports which were inaccessible to me and which were collected by Siemens in 1925. He gave full data only on the families in which more than one child was affected; hence, when these cases were included in my analysis without the corresponding data on families in which only one child was affected the results sometimes appeared to be in disagreement with the conclusions derived from the smaller series. This will be taken up in detail later.

If xeroderma pigmentosum is dependent on a pair of recessive determiners located in one pair of chromosomes, one would expect approximately one fourth of the offspring to be affected, as two parents both of whom are hybrids for the condition, and are outwardly normal, will produce children in the proportion of one-fourth normal, one-fourth affected and one-half hybrid like themselves. This proportion may be expressed by the formula $N X \times N X = N N + 2N X + X X$, in which N stands for normality and X, for the presence of xeroderma pigmentosum and N suppresses the appearance of X. But as many families have less than four children and are included in the series

TABLE 2.—*Data on Families with Xeroderma Pigmentosum in Which Adequate Information Was Given*

Number in Family	Number of Families	Total Number of of Children	Total Number of of Children Affected	Number of Children Expected to Be Affected
1	12	12	12	12.0
2	12	24	15	13.7
3	19	57	29	24.6
4	21	84	36	30.6
5	14	70	26	22.8
6	12	72	28	21.9
7	9	63	19	18.1
8	11	88	23	24.4
9	8	72	21	19.4
10	4	40	9	10.6
12	2	24	6	6.2
13	1	13	7	3.3
14	1	14	2	3.6
16	1	16	2	4.0
Total	127	649	235	215.2

* The average number of affected children in each family was 1.85 ± 0.05. The average number of children which should have been affected in each family is 1.7. The difference between the two averages is 0.15, which is three times the probable error, 0.05. This discrepancy is due to the fact that this list is weighted by the inclusion of a large number of families in which two or more children were affected and by the exclusion of the families in which but one child was affected. In the original series of 170 cases collected before I added the cases in Cockayne's list, almost perfect agreement was shown between the theoretical and the actual number of children affected, as discussed in the text.

because they have at least one affected child, the proportion of affected to normal children is always higher than the theoretical 1 : 3. In the 170 case reports which I collected in which adequate data were given the ratio of affected to normal persons was 1 : 1.9. When Siemens' cases were added the ratio was 1 : 1.75, both ratios being much too high. One cannot tell how many parents in the community were capable of producing affected offspring but had only normal children; so one cannot include the normal children of these families to bring the proportion of normal subjects up to its correct figure. By the use of appropriate mathematical formulas allowance can be made for this undue number of affected offspring.

In table 2 are arranged the data on all the families on which the requisite amount of information was given, namely, the total number

of children in the family and the number of affected children. For only 127 of the 198 families listed in table 1 did I have adequate data as to the number of normal and affected offspring. In the fourth column of the table is given the number of children actually affected in families of the different sizes, while in the last column of this table is stated the number of children who would be expected to be affected in this number of families of any given size if the disease were dependent on recessive determiners and the parents were normal, as they were in all instances. These percentages are derived by appropriate mathematical formulas. It will be seen that the totals of the columns for the number of children actually found to be affected and the number of children who would be expected to be affected are 235 and 215.2, respectively. The average number of affected children in a family is 1.85 ± 0.05. The average number of children expected to be affected in a family according to the formula is 1.7. The difference between the two averages is 0.15, which is three times the probable error.

But it must be remembered at this point that the cases which were added from Cockayne's list were all instances in which more than one child in a family was affected. He gave no data on 50 cases in which but one child in the family was affected and the total number of normal sibs was 151. In 87 other instances the original record gave no information. The exclusion of these cases makes the total number of affected children and the average number in a family differ greatly from the theoretical expectation. In the original 170 cases which I collected and which were not weighted in favor of any one type, the total number of affected children in families on which adequate data were given was 103, and the total number who would be expected to be affected, according to the theory, was 101.36. The average number of affected children in a family was 1.68 ± 0.09, and the average according to the theory was 1.66. In this series of cases the difference between the actual and the theoretical figure was 0.02, which is less than one fourth of the probable error, 0.09. The disagreement between the results obtained when the original 170 cases were used and those which were derived after the cases listed by Cockayne were added is due to the fact that the figures for the latter group were unduly weighted in favor of the instances in which more than one child was affected in a family.

This can be seen by referring to table 1. It will be noted from this table that there were 3 two child families in which both children were affected. There were 9 two child families in which but one child was affected. According to expectation, there should have been approximately 18 families of the latter class, or the number of two child families in which one child was affected should have been six times as great

as that of similar families in which both children were affected. There were 8 three child families with but one child affected, when there should have been about 27 families of this type. Similar figures could be given for the rest of the sibships. Thus, there was but 1 six child family with one child affected, when there should have been 15 in proportion to the rest of the six child families. Some of these missing families were those with one child affected on which Cockayne did not give the data, and if they had been included no doubt the results in table 2 would have been in as close agreement as the results for the series of 170 cases, data on which were originally collected.

TABLE 3.—*Results of Statistical Treatment of Data on 170 Families in Which Xeroderma Pigmentosum Appeared*

s	n_s	r_s	$s.n_s$	q^s	$1 - q^s$	$\frac{s.n_s}{1 - q^s}$	Corrected Value for p
1	7	7	7	0.750000	0.2500	28.0	25.0
2	8	10	16	0.562500	0.4375	36.5	27.4
3	8	10	24	0.421875	0.5781	41.5	24.1
4	10	17	40	0.316406	0.6836	58.5	29.0
5	6	8	30	0.237304	0.7627	39.3	20.3
6	5	12	30	0.177978	0.8220	36.5	32.8
7	5	11	35	0.133484	0.8665	40.3	27.2
8	6	11	48	0.100113	0.8999	53.3	20.6
9	2	2	18	0.075085	0.9249	19.4	10.3
10	1	3	10	0.056313	0.9437	10.6	28.4
12	1	3	12	0.031676	0.9683	12.4	24.2
13	1	7	13	0.023757	0.9762	13.4	52.2
16	1	2	16	0.010022	0.9899	16.1	12.5

In this table s indicates the number of children in the family; n_s, the number of families with s number of children; r_s, the number of affected children in these families; $s.n_s$, the number of children, both affected and normal, in these families, and q^s, the proportion of normal children expected in a family in which the defect is due to a single recessive gene substitution.

The corrected value for p, which should equal 25, or the percentage of children expected to be affected, is derived from the formula $\frac{\frac{r_s \times 100}{s.n_s}}{1 - q^s}$

The average of the corrected values for p in the last column is 25.7 $\pm$ 1.6. Thus, the probable error of the corrected value for p is less than the difference between this value and the theoretically correct value, 25.

This table was based on the data on the 170 cases originally collected, without the addition of the cases cited by Cockayne.

A second method of ascertaining the agreement between the theoretical and the actual figures, if the condition is dependent on recessive factors, is the use of the formula of Hogben. The results of this method are shown in table 3. Here only the original 170 cases were used, for they had not been selected on a familial basis only and so gave a truer picture of the actual ratio of affected and normal children. If all the families which might have had affected children are included, the average percentage of affected children is 25, indicated by p. Since some of the families were omitted, owing to the fact that they did not have an affected child, the actual percentage of affected children must be corrected. The corrected value for p should be 25 to have perfect agreement between hypothesis and fact. Since the number of families with

one, two or three children is too small for perfect agreement between the theoretical and the actual value for p for each size fraternity, the average value for p for the whole series must be calculated. The average value of p as determined from the last column, table 3, is 25.7 ± 1.6. The difference between 25 and 25.7 is 0.7, which is less than one half of the probable error, 1.6. Therefore, this method again substantiates the hypothesis that xeroderma pigmentosum is dependent on recessive determiners.

THE SIGNIFICANCE OF COUSIN MARRIAGES

If these statements are correct, namely, that this condition is inherited and that it is dependent on recessive factors and if the sexes are about equally affected, as they are found to be from an analysis of the data in table 1, one would expect to find that the parents of patients with xeroderma pigmentosum are related more frequently than parents in the general population. The matter will be discussed at this point to show that the incidence of consanguineous matings among the parents of affected offspring has a bearing on the question of inheritance of disease.

Let it be supposed that there are two boxes, one on the left, with 99 black cubes and 1 white cube, and a second on the right, containing 50 white and 50 black cubes. The subject takes a white cube from another pile, and being blindfolded so that he chooses at random, he takes a cube from the box on the left. What is the chance that he will hold 2 white cubes in his hand? It is only 1 : 100, since there are ninety-nine times as many black as white cubes to be selected. Now the second cube is selected from the box on the right. The chance of holding 2 white cubes in the hand is now 1 : 2, since he is just as likely to choose a white as a black cube, the number being equal.

Certain characters may be substituted for the colored cubes. It may be supposed that a black cube represents a person whose skin is normal and who has no factors for xeroderma pigmentosum. A white cube represents a person whose skin is normal but who carries a latent factor for xeroderma pigmentosum. When 2 black cubes or a black and a white cube are held in the hand, they represent matings in which the children can never have this cutaneous disease; but when 2 white cubes are held simultaneously, it represents a mating in which it is possible for the disease to develop in the offspring. The box of cubes on the left represents the general population, in which in my illustration 1 person in every 100 carries a latent factor for xeroderma pigmentosum. The actual number of persons carrying this latent factor is much less than this, and this figure is used merely as a convenient illustration.

The box on the right represents the relatives of the person who carries this latent factor for xeroderma pigmentosum. The much higher proportion of relatives carrying this latent factor is explained by the fact that related persons come from the same germ plasm in part and hence are far more likely to have the same traits than are unrelated persons.

If the person with a latent factor for xeroderma pigmentosum marries a person from the general population (represented by the box on the left) he has 1 chance in 100 of picking a mate with the same trait in latent form. If he mates with a cousin (represented by the box on the right) he has 1 chance in 2 of mating with a person carrying this latent factor. Hence, if he marries a cousin, he is fifty times as likely to have offspring who show xeroderma pigmentosum as though he mates with an unrelated person. Therefore patients with xeroderma pigmentosum are much more likely to come from cousin marriages than from marriages between unrelated persons. If this disease is inherited as a recessive character and a series of instances of the condition is collected, the proportion of cousin marriages should be found to be much higher than that in the general population. Conversely, if a series of cases of any disease is collected which is not known to be inherited and an excess of cousin marriages is found among the parents, one is justified in concluding that the disease is hereditary and that it is transmitted as a recessive condition. An excess of cousin marriages among the parents of patients with such a disease as compared with the percentage of consanguineous matings in the population does not mean, however, that the persons with this disease are more likely to mate with cousins than are other persons who do not have this latent factor.

An illustration will make this point clear. If it were found that parents of patients with xeroderma were related fifty times as often as parents of persons not showing xeroderma, one might be tempted to conclude that some selective factor is at work which induces cousins having the latent trait for xeroderma to marry and to produce affected offspring. The illustration of the boxes of cubes may again be used. To begin with, it is known that about 1 marriage in every 500 in the general population is between cousins; that is, 0.2 per cent of matings are consanguineous. Now with the white cube in the hand, representing a person who carries the latent trait for xeroderma the subject makes 10,000 choices from the box on the left, which indicates the general population. Since 1 per cent of the choices are likely to fall on the white cube, there are 100 matings between persons with the latent trait for xeroderma and hence 100 matings which may produce affected offspring. Since a person is five hundred times as likely to choose an unrelated as a related mate, 20 choices may be made from the box on

the right for the 10,000 from the box on the left. But of these 20 choices 10 are likely to fall on the white cube, or, in terms of persons, 10 of the 20 matings are likely to be with cousins who have the same trait latent. Therefore these 10 matings result in affected offspring. Thus, of 110 matings in which affected offspring were produced 10, or about 9 per cent, were consanguineous marriages.

As is evident from the experiment, persons with this trait latent do not marry a relative with any greater frequency than persons without this trait, but marriage with a relative having been made, the trait is much more likely to appear. Hence it is found that in a large series of cases cousin marriages are unduly frequent among parents whose offspring show an inherited recessive condition. It has been assumed in this discussion that in this theoretical population xeroderma pigmentosum is inherited as a recessive character, and it is found as a result that cousin marriages occur with great frequency. In actuality one must approach the problem from the other end and find whether there is an excess of cousin marriages and if so, one must reason back to the assumption that the trait in question must be inherited and transmitted as a recessive character.

It must be remembered, however, that the incidence of consanguineous matings is disproportionately high among parents of persons exhibiting inherited recessive traits only when the traits are relatively rare. The more common the trait the nearer the incidence of consanguineous matings approaches that found in the general population, since if the trait is universal one is as likely to find it among unrelated as related persons.

INCIDENCE OF COUSIN MARRIAGES

The observed percentages of children affected with xeroderma pigmentosum in a family having been found to agree closely with the percentages which would be expected if the disease were dependent on a pair of recessive determiners, it may now be ascertained whether there is an undue percentage of consanguineous matings among the parents of the children with this disease, thus furnishing another criterion by which the validity of the hypothesis is tested. Toyama expressed the belief that consanguineous matings play an important rôle in causing this disease. According to Ormsby, he described over 30 cases in Japan and found that cousin marriages were frequent among the parents of the patients in his series.

The 361 cases listed in table 1 occurred in 198 families. There were 26 instances of first cousin marriages, 10 of second cousin marriages and 1 of marriage between first cousins once removed. In 5 instances the parents were related, but the degree of relationship was not mentioned. Thus, the incidence of consanguineous matings was 21.2 per

cent. The average incidence of marriages between relatives in the general population varies in different localities, but it has been estimated by Baur, Fischer and Lenz to be about 0.2 per cent. In families in which xeroderma pigmentosum appears the parents are related about one hundred and six times as frequently as parents in the general population.

If one considers the incidence of cousin matings only when a statement was made as to the relationship between the parents, it is found that in 42 of the 60 instances in which this point was mentioned in the record there was a history of parents who were related, or an incidence of 70 per cent of consanguineous matings. This estimate is no doubt too high, for even if the inquiry as to relationship were made, the tendency would be not to include a statement unless the questioner obtained what he considered a positive answer. The real incidence of cousin marriages among the parents of patients with xeroderma pigmentosum is probably more than 21 per cent and less than 70 per cent. The high percentage of consanguineous matings among the parents of these patients confirms the idea that xeroderma pigmentosum is inherited and that it is dependent on recessive determiners.

The conclusion having been reached that this disease is inherited as a recessive character, the following statements must be examined critically, for the laws of inheritance do not support any of these assertions: (1) The disease usually affects more than one in a family; (2) only one sex in a family is affected, and (3) all the members of that sex are affected in that family. With regard to the first statement, of the 198 families listed in table 1, 82 families had one child affected and 116 had more than one. But this table includes all the cases which had been collected by Siemens up to 1925 in which more than one child was affected and none of his cases in which but one child in the family was affected. Siemens had collected prior to 1925 146 cases in which one child was affected. In my original series of 170 cases 50 instances of this type occurred before 1925. Even if all of these instances were identical with 50 cases in Siemens' list, there were at least 96 such instances prior to 1925 which should be added to the figures just cited. Thus the corrected list would show 178 families with one child affected and 116 families with more than one child affected. This means that 60 per cent of all families in which xeroderma pigmentosum appeared had only one child affected and 40 per cent more than one. This is the same ratio that was found in my series of 170 cases. The cases in my series occurred in 108 families, in 65 of which one child only was affected and in 43 more than one child. In this series also the incidence of families in which one child was affected was 60 per cent. Hence,

it can be stated that, contrary to the statements concerning this disease in the textbooks, the majority of families do not have more than one child affected.

This statement sounds paradoxical, for if a disease is inherited would not one expect to find more than one child exhibiting it in any family? One would not if the disease is due to a recessive determiner. Small families are far more common than large, and it is not until families of six children or more are considered that one expects to find a greater proportion of families having two or more children affected than of families having only one with the disease. Thus, one expects to encounter six times as many two child families in which one child is affected as similar families in which both children show the condition. In the group of three child families 27 families with one child affected will be found to every 10 families with more than one child affected, and so it goes until the group of six child families is reached, in which 1,909 families with more than one child affected are expected for every 1,458 families with but one child who has the disease.

In table 2 it is found that of the 127 families in which the total number of offspring was given, 78 families, or 61 per cent, had less than six children and only 39 per cent more than six. Therefore if the majority of families have five children or less and if more families of that size are likely to have one child affected than to have several, it is obvious that as a rule one child only in the family will be affected. The larger the number of children the more likely is the family to have a second child affected. Despite the fact that families with less than six children are less likely on the whole to have several children than to have one child affected, the possibility that a second child may be affected should always be borne in mind in giving advice to parents concerning the rearing of more children after one has fallen victim to this tragic disease.

Thus, although more small families will have only one child affected than will have more than one, the possibility that more than one child will be affected is by no means remote. On the average, one seventh of two child families in whom this disease appears will have both children affected. One fourth of the three child families in whom this disease appears will have two of the three children affected, and in 1 of every 37 families of this size all three children will be affected. Hence, there is danger in assuring parents that they will not have a second child with the disease.

The statement that one sex only is likely to be affected in a family may now be examined. To examine this assertion critically, one must use only the families in which at least two children were affected and

there was thus a chance for one child of each sex to show the condition. Of the 114 families with more than one child affected both sexes were affected in 52, or 45.6 per cent. In 8 other families in which one sex only was affected but one sex was represented in the family, and hence there was no possibility for both sexes to be affected. In 4 families only boys were affected and in 4 only girls. Thus, in 60 families, or 52.6 per cent, the rule that the disease did not affect both sexes in the family was broken. In 21 other instances in which two sisters or two brothers were affected no statement was made as to whether there were any other children of the opposite sex in the family who may have been affected, and in 8 instances the sex of all the affected children was not given. Apart from these last instances, however, it can be stated that a rule that is followed less than half the time can scarcely be called a rule. The statement that the disease affects one sex only in a family was made on the basis of a few families, and it has been repeated again and again, with no basis in fact. If the disease is caused by a recessive determiner that is not sex linked, it should not be expected to affect one sex only in a family as a rule. I find that the facts support my interpretation as to its inheritance.

The third point will be considered, namely, that not only is one sex alone affected but all the members of one sex in any family tend to be affected. One hundred and ninety-eight families are listed in table 1. From this list must be excluded all one child families, all families in which both sexes were affected and all families in which the affected child was the sole member of that sex in the family. When one considers only the families in which one sex only was affected, those in which at least two of that sex in the family had the disease and those in which the sex of all the unaffected children was given, there are 53 families by which the validity of the rule can be tested.

In these 53 families this rule was followed in 10 instances and broken in 43. A rule that is followed in but 19 per cent of the cases can scarcely be called a rule. It might be claimed that if for all the families with an inadequate family history more data had been given as to the sex and number of normal children in the family, the 10 cases just cited might have been augmented. As the authors who made the statement that all the members of one sex tend to be affected in any given family had no more data on these families than I possess, since they had only the written records on which to rely, it is safe to state that this idea is erroneous and is not borne out by facts. This result is what one would expect, for if xeroderma pigmentosum is inherited as a recessive disease and not as a sex-linked or sex-limited character, there is no known genetic mechanism by which all the members of one sex in one family are affected while the other sex is left untouched.

SUMMARY

1. Contrary to statements made in textbooks of dermatology, xeroderma pigmentosum is found to be inherited, the determiners for which are passed on in the germ plasm from parent to child.

2. It is transmitted as a recessive condition; hence parents who are normal themselves may produce affected offspring.

3. Consanguineous marriages are found far more frequently among parents of patients with xeroderma pigmentosum than among the general population, the minimal incidence being 21.2 per cent in the series collected.

4. The two sexes are affected equally; hence there is no sex linkage.

5. There is no tendency for the disease to pick out one sex in any family and to leave the other unscathed.

6. Because of the average small size of families, there are more families with one child affected than those with more than one. This does not preclude the possibility or even probability that in any family a second child may be affected.

7. There is no support for the statement that the disease, having affected one sex in the family, affects all the children of that sex in the family. It affects males and females equally and may affect both sexes in the same family.

8. It is to be hoped that practitioners, when recording the family history in cases of disease which they term familial, will include in their data (1) the number and sex of the affected children, (2) the number and sex of the normal brothers and sisters, (3) a definite statement as to whether or not the parents were related, (4) any history of the disease in former generations and (5) the age at which the normal brothers and sisters died, or were living at the time of recording, so that, if the disease is one which does not begin until several years after birth, all the children who died in infancy or had not yet attained the minimal age of onset can be excluded from the final record. Such data will take little time or space and will make the record valuable not only for clinical purposes but for genetic study.

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EXFOLIATIVE DERMATITIS

REPORT OF A CASE WITH AUTOPSY

THOMAS BUTTERWORTH, M.D.
READING, PA.

Although death from exfoliative dermatitis is not uncommon, there are comparatively few reports of cases in which autopsy has been performed. In 1933 Poole and Wehger [1] found seventeen reports of cases in the literature and contributed four more. To these may be added the case reported by Allison [2] and that by Nelson,[3] making a total of twenty-three cases recorded in which autopsy was performed.

The pathologic changes described in the reports of cases have varied greatly. No particular organ or combination of organs has been uniformly involved. The lungs have been the most frequent site of involvement, presenting the following conditions, named in the order of frequency: bronchopneumonia, desquamation of the bronchial mucosa, edema, hemorrhagic infarcts and multiple abscesses. Fatty degeneration and cloudy swelling have been the most frequent changes noted in the liver. The kidneys have been described as being large and pale, with multiple hemorrhages or tubular desquamation. Submucosal hemorrhages, with or without ulceration, were frequently observed along the gastro-intestinal tract. The changes in the spleen have apparently been of minor importance; simple hyperplasia, which occurred three times, and chronic passive congestion, twice. Aplastic bone marrow and acute diffuse myocarditis were each noted in one instance.

As the pathogenesis of exfoliative dermatitis remains unknown, the recording of isolated cases in which autopsy has been performed seems warranted, in the hope that an accumulation of evidence may lead to an understanding of the underlying pathologic process of the disease. The case described in this paper has added significance in that the patient was recovering from the dermatitis when he suddenly died of coronary sclerosis. It is reasonable to believe that the acute pathologic change

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From the Department of Dermatology and Syphilology of the Reading Hospital.

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observed in postmortem examination is an indication of the pathologic change occurring in the person who recovers uneventfully.

REPORT OF CASE

W. B. R., a white man aged 26, was admitted to the Reading Hospital on Nov. 14, 1935. He had enjoyed good health until May 1935, when he observed that drinking milk in any form was followed by nausea, vomiting, fever and occasionally headache. His physician prescribed a "tonic" and advised him to avoid milk and its products and to adhere to a vegetable and fruit diet. Several weeks later he noted the appearance of flat, light tan, slightly raised oval patches on the skin of the abdomen, chest, back and neck.

Despite scrupulous adherence to the diet, he suffered from frequent attacks of nausea and vomiting in the summer months that followed. However, he was able to continue his usual occupation. In the meantime the eruption was gradually disappearing. In September he suffered from pains about the heart and was bedfast for two days. At that time he began taking three kelpamalt tablets[4] daily. About October 3 there suddenly appeared a generalized scarlatiniform rash, accompanied by headache and low grade fever but not by nausea, vomiting or sore throat. He was confined to bed. The bright red color gradually faded and was followed by diffuse scaling. The scales were fine at first but later became large, resembling soap chips. Two weeks prior to the patient's admission to the hospital, the skin of the back became moist. The disease process had been moderately pruritic since its inception.

The patient had always been weak. When a child he had suffered from measles, whooping cough, scarlet fever and chickenpox. There was a vague history of the occurrence of rheumatic pain in one knee. He underwent a tonsillectomy at the age of 13. There was no history of a previous cutaneous disorder or of venereal disease, nor had he ever had an intravenous injection.

The patient's father died at the age of 50, of gastric carcinoma. His mother, two brothers and three sisters were living and well. There was no history of tuberculosis or of allergic disease in the family.

The patient was employed in the wood working department of an iron company. In addition, he did considerable professional painting, using oils, water colors and charcoal. He was single and lived with his mother.

Physical Examination.—On examination the patient appeared to be asthenic. He seemed comfortable, was cooperative and answered questions intelligently. There was no evidence of cyanosis or jaundice.

The skin of the entire body, except that of the palms and soles, was reddened and covered with laminated papery scales. The scalp and beard were covered with a yellowish crust. The skin of the upper part of the back was moist and oozing, but other portions of the trunk and extremities were dry. The nails were opaque gray, with irregular transverse ridges. The mucous membrane of the eyes, mouth and throat was inflamed. Secondary excoriations with hemorrhagic crusting were present on the extremities, particularly on the buttocks and arms.

The pupils were round, regular and equal and reacted to light and in accommodation. Extra-ocular movements were normal. The conjunctivae and scleras were

4. Kelpamalt, which consists of specially dehydrated kelp, malt extract, powdered milk and chocolate, contains the following minerals: calcium, phosphorus, iodine, magnesium, iron, copper, sodium, potassium, manganese, aluminum and sulfur.

of normal color. There was bilateral chronic otitis media with perforation and granulation tissue, especially on the right. Bilateral ethmoiditis was also present, but the tonsils appeared to be normal.

Expansion of the chest was fair and equal on the two sides. The percussion note was resonant throughout, and the breath sounds were normal. The size of the heart was within normal limits. The heart sounds were of fair quality and regular in rhythm. There were no murmurs or thrills. The blood pressure was 116 mm. systolic and 76 mm. diastolic.

The abdomen was tympanitic throughout. There were no palpable masses or tenderness.

The deep reflexes were normal. All the superficial lymph glands were discretely enlarged.

A diagnosis of generalized exfoliative dermatitis (Wilson-Brocq) was made.

Laboratory Data.—The sugar content of the blood was 110 mg. and the nonprotein nitrogen content 37 mg. per hundred cubic centimeters. The Wassermann and Kahn tests of the blood gave negative results. The blood count revealed 4,160,000 red corpuscles, with 79 per cent hemoglobin. The white cells numbered 22,700, with 38 per cent polymorphonuclears, 11 per cent lymphocytes and 51 per cent eosinophils. The urine showed a faint trace of albumin, with from 40 to 50 white cells per high power field.

Course.—During his stay in the hospital, the patient's temperature varied from 97 to 99.6 F. and his pulse rate from 75 to 135. Treatment consisted in frequent colloid baths, large doses of calcium lactate by mouth, iron and ammonium citrate taken internally and the daily intravenous injection of 250 cc. of a 10 per cent solution of dextrose and of 8 units of insulin hypodermically. Under this regimen there was rapid improvement of the dermatitis. The scaling diminished, and the skin became less red. There was less itching; the patient's appetite improved, and he was rapidly regaining strength. Suddenly he died, on the morning of the ninth day in the hospital.

Postmortem Examination.—Autopsy was performed by Dr. Erwin D. Funk, two hours after death.

The peritoneum was pale, smooth and glistening and contained no excess of fluid. The intestines were collapsed, except for a small amount of feces. The appendix was normal, measured 18 cm. in length and presented no adhesions. It was retrocecal and pointed toward the liver. The cecum was mobile and located in the pelvis. The omentum was thin and filmy; it contained little fat and covered the intestines well.

The left pleural cavity presented some light adhesions anteriorly. The left lung measured 18 by 16 by 5 cm. and weighed 210 Gm. It was pale light gray, with few anthracotic markings. It was crepitant throughout. No congestion or edema was present. The right lung measured 20 by 17 by 5 cm. and weighed 260 Gm. It resembled its fellow in every respect.

Histologic sections of the lungs showed alveoli normal in size, except in a few areas of partial atelectasis. The alveoli were free from exudate or transudate. The interalveolar capillaries were not engorged. The bronchi were collapsed and free from secretion. The pleural surface presented no abnormalities.

The pericardium was normal and contained a small amount of clear straw-colored fluid. The heart in situ extended 3 cm. to the right of the midsternal line in the third interspace and 8 cm. to the left of the midsternal line in the fifth interspace. It measured 12 by 9 by 4.5 cm. and weighed 240 Gm. On the posterior wall of the left ventricle there was an area of old fibrosis, which sug-

gested that of an old healed infarct. The left coronary artery was closed by a fibrous cord, 1 cm. in length, extending distally from a point 1.5 cm. beyond the sinus of Valsalva. The right coronary artery presented some ulcerative plaques, which almost occluded the lumen of the descending branch. The left ventricular wall was 1.5 cm. thick and the right ventricular wall 0.6 cm. The aortic valve measured 6.5 cm. in circumference and contained yellow atheromas in the sinus Valsalva. The leaflets were thin and competent. The pulmonary valve measured 6 cm. in circumference and was normal. The mitral valve measured 8.5 cm. and showed slight thickening at the base. The tricuspid valve measured 12 cm. and was normal. The aorta was marked with numerous atheromas.

Sections of the cardiac muscle of the left ventricle showed approximately one-third replacement by fibrous tissue, which was irregularly distributed throughout the section. In many small areas the remaining muscle cells had become cloudy, stained poorly and had indistinct nuclei. The fibrosis extended into the papillary muscles. The epicardial and endocardial surfaces were clear. Sections of the left coronary artery showed an atheromatous process, involving the entire media and encroaching on the lumen, so that it was reduced to less than one fifth of its normal extent. The lumen was eccentric but lined with normal endothelium. The involved portion of the media showed many areas of cholesterol crystals and additional areas of calcium deposition. The lumen contained no thrombus. Sections of the aorta showed an active atheromatous process and no specific destruction of elastic fiber elements.

The liver measured 30 by 19 by 7.5 cm. and weighed 1,490 Gm. The surface was pale bluish, smooth and glistening. The cut surface had a pale yellowish tinge on a reddish-brown background.

Sections of the liver showed undisturbed lobular architecture. The hepatic cells were swollen, their cytoplasm granular and their cell membranes indistinct. Throughout the lobule the cells contained many fat globules in the cytoplasm. The blood sinusoids were not engorged. The Kupffer cells were well preserved.

The spleen measured 14 by 10 by 5 cm. and weighed 340 Gm. The surface was smooth, wrinkled and dark purple. The cut surface showed a soft pulp with increased fibrosis.

Sections of the spleen showed somewhat enlarged malpighian bodies, but there was no hyperplasia of the reticulum cells. The pulp was greatly congested; all the blood sinusoids were engorged. Eosinophils were particularly noticeable in these sections. An increase in the fibrous tissue and pigment of the organ was not present.

The left kidney measured 12 by 5.5 by 4 cm. and weighed 190 Gm. The capsule was smooth and pale and stripped with ease. The exposed cortical surface was pale grayish red. The cut surface was pale grayish and bulged from beneath the capsule. The ureter was single and patulous. The right kidney measured 12 by 6 by 3.5 cm. and weighed 170 Gm. It resembled its fellow in every respect.

Sections of the kidney showed a diffuse dense infiltration of the stroma by lymphocytes. These cells seemed equally distributed in the cortex and medulla, and the arrangement did not suggest a specific etiology. Within the cortex were a few scars containing fibrosed glomeruli. An old organized complete thrombus occupied one of the larger arterial branches. The remaining glomeruli showed no change. The tubule cells were swollen, and many had undergone hydropic degeneration.

The prostate gland, gallbladder, stomach, small intestine and pancreas were found to be normal, on both gross and histologic examination.

The large intestine was normal, except for the presence of a dark red polyp, the size of a cherry stone, in the cecum. Histologically the growth was composed of glandular structures, resembling normal intestinal glands, supported by congested and edematous stroma and infiltrated by leukocytes of all kinds. All the surrounding intestine was normal.

SUMMARY

A case of exfoliative dermatitis of undetermined etiology with observations made at autopsy is recorded. The dermatitis was responding favorably to treatment when the patient died suddenly of coronary sclerosis.

The chief observations at autopsy were as follows: healed infarction of the myocardium with atheromata of the left coronary artery, causing almost complete obstruction; atheromatous plaques of the aorta; cloudy swelling, passive congestion and early fatty degeneration of the liver; arterionephrosclerosis, cloudy swelling and chronic pyonephritis of the kidneys, and passive congestion and mild hyperplasia of the spleen.

238 North Fifth Street.

Clinical Notes

FILTERED ULTRAVIOLET RAYS

An Inexpensive Unit for Their Isolation

GEORGE M. LEWIS, M.D., AND MARY E. HOPPER, M.S., NEW YORK

The phenomenon of fluorescence noted in many substances when they are observed under filtered ultraviolet rays is of great value to the dermatologist. Margarot and Devèze [1] first drew attention to the value of the rays as a diagnostic measure in infections of the scalp with Microsporon. Other observers [2] have confirmed their observations.

The use of the rays has been extended to many different medical and other scientific fields. In dermatologic practice the important fluorescent effects noted when the filtered ultraviolet rays are used as a sole source of light may help to detect pathologic conditions and to differentiate fungi in cultures.

1. In cases of tinea capitis the value of the rays cannot be overstressed, not only in establishing a diagnosis but as an aid in following the progress of the disease and of determining when cure has taken place. Furthermore, in certain infections with Microsporon Audouini when regrowth of hair is considerable the diagnosis of tinea capitis may not be suspected. In such instances, when only scaling of the scalp may be noted, fluorescence of the affected hairs is characteristic. Patients with this condition before the disease is recognized constitute a serious menace, as they are potential foci for dissemination to other children.

(*a*) In all types of infections due to Microsporon the affected hairs appear as luminous short yellowish green "stubs."

(*b*) In infections with Trichophyton endothrix the affected hairs are dull and bluish. This observation [3] is not in agreement with that of Davidson and Gregory,[4] who stated that hairs infected with Achorion Schoenleinii fluoresce like those infected with Microsporon and that all the hairs infected with Trichophyton do not fluoresce. It is true that hairs present in follicles invaded by Trichophyton

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From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University, George M. MacKee, M.D., Director.

1. Margarot, J., and Devèze, P.: Aspect de quelques dermatoses en lumière ultraparaviolette—note préliminaire, Bull. Soc. d. sc. méd. et biol. de Montpellier **6**:375 (June) 1925.

2. Goodman, H.: Fluorescence, Particularly in Dermatology, Brit. J. Dermat. **40**:105 (March) 1928. Cleveland, D. E. H.: "Wood Light" in Dermatologic Diagnosis with Special Reference to Ringworm, Arch. Dermat. & Syph. **18**:368 (Sept.) 1928.

3. Lewis, G. M.: Ringworm of the Scalp: Curability, Without Depilating Measures, of Infections Caused by "Animal" Microsporons, Am. J. M. Sc. **189**: 364 (March) 1935.

4. Davidson, A. M., and Gregory, P. H.: Note on an Investigation into the Fluorescence of Hairs Infected with Certain Fungi, Canad. J. Research **7**:378, 1932.

ectothrix do not fluoresce, but in our experience in every case of infection with Trichophyton violaceum (endothrix) fluorescence of the infected hairs was a useful observation.

(*c*) In infections with A. Schoenleinii the color is greenish but less luminous than in the infections with Microsporon.

2. Animal carriers (particularly kittens) of certain pathogenic fungi may be detected [5] by fluorescence of affected hairs which when observed under filtered ultraviolet rays have an appearance identical with that of human hairs affected with the disease.

3. Various fungous growths in culture may be distinguished [6] by their characteristic fluorescent colorations.

4. Tinea versicolor and erythrasma show individualistic colors sufficient not only to establish the correct diagnosis but to determine the extent of the eruption even when it has faded so that its presence cannot be clinically detected.[7] Other fungous eruptions, such as tinea circinata, tinea cruris, dermatophytosis of the feet and the secondary eczematous and dyshidrotic eruptions of the hands and other parts, infections with Monilia as well as the deep fungous infections (sporotrichosis, actinomycosis, blastomycosis, coccidioidal granuloma, etc.) do not fluoresce in any characteristic fashion when observed under filtered ultraviolet rays.

5. Hairs affected by lepothrix fluoresce.

6. Keratin fluoresces, and when it is increased more luminosity may be seen. The palm is brighter than the dorsum of the hand. Normal teeth and nails fluoresce brilliantly. The differentiation of certain diseases of the nails is being investigated by us at the present time. Warts and keratoses show a bright fluorescence, while molluscum bodies exhibit a dark center.

7. Some fading and indistinct eruptions become clearer when observed under filtered ultraviolet rays.[8] An accentuation of the syphilitic roseola is frequently apparent, and this finding is useful when the diagnosis is not easily made, particularly when concomitant findings are absent. Lentiginous and pigmented lesions usually appear darker when seen under filtered ultraviolet rays than when observed in ordinary light.

8. Many inorganic substances fluoresce. When a drug such as salicylic acid or a product such as petrolatum is present on skin examined under filtered ultraviolet rays the underlying condition may be masked.

Since filtered ultraviolet rays are of such importance, a suitable unit for their isolation not only appears to be a necessary part of every dermatologist's equipment but should also prove a useful aid to the general practitioner. The following discussion covers the more essential details and offers suggestions for the construction of an inexpensive unit for attachment to an ultraviolet lamp.

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5. Davidson, A. M., and Gregory, P. H.: Kitten Carriers of Microsporon Felineum and Their Detection by the Fluorescence Test, Canad. M. A. J. **29**:242. 1933.

6. Lewis, G. M.: Fluorescence of Fungus Colonies with Filtered Ultraviolet Radiation (Wood's Filter), Arch. Dermat. & Syph. **31**:329 (March) 1935.

7. Lewis, G. M., and Hopper, M. E.: Pseudo-Achromia of Tinea Versicolor, Arch. Dermat. & Syph., to be published.

8. Meyer, J., and Saidman, L.: Application of Wood's Light to Dermatologic Diagnosis, Bull. Soc. franç. de dermat. et syph. **32**:369, 1925.

SOURCE OF ULTRAVIOLET RAYS

As a rule, it is not practical to use the sun's rays as a source of ultraviolet rays. However, any of the ordinary office lamps for the production of ultraviolet rays, whether air cooled or water cooled, is suitable for this purpose. Less expensive lamps are also serviceable although the heat generated is a drawback. Davidson and his co-workers [9] have devised two different lamps which are portable and have proved satisfactory for the detection of tinea capitis. The directions given for their construction, however, are rather vague in certain particulars. Another source of light is a commercial lamp used for indoor photography in which there is an overloaded filament to produce the requisite bright light, with a correspondingly shorter life than with ordinary lamps. Although the content of optimum rays from its beam is not so great as that of the beam of the aforementioned lamps, it is nevertheless a satisfactory substitute for an ultraviolet lamp. It may also be used to differentiate fungous growths in culture.

FILTER

The type and thickness of the glass filter through which the ultraviolet rays pass are of great importance. This is especially true in observations on the fluorescent colorations of cultures of fungi. Divergent results may be obtained by different observers owing to a difference in the type of glass filter or in its thickness. We have found that the wave lengths in the near portion of the ultraviolet part of the spectrum (in the region of 3,650 angstrom units) offer optimum fluorescent value. Many different types of glass have been tried; the Corning glass violet ultra,[10] no. 586, polished to a thickness of between 4 and 5 mm. is adequate for use. In its molded form it is usually from 7 to 8 mm. in thickness, and unless the source of light is extremely powerful, not enough ultraviolet rays are transmitted to produce the desired results. This filter is a sodium barium silicate glass and contains slightly less than 9 per cent nickel oxide. As the glass is not heat resistant care must be exercised that overheating does not take place, or cracking will result.

EXCLUSION OF UNWANTED RAYS

The room in which the examination is made must be darkened, and in addition most of the visible rays from the ultraviolet lamp must be excluded by a suitable attachment so that only rays of light from the lamp which are not absorbed will pass through the filter. A tinsmith's services may be utilized, or a molded copper attachment may be fitted to the lamp, leaving an open slot for the filter.[11] The disadvantages of such a device are (1) that the attachment is not transferable to a different make of lamp or, often, to a different model of the same make of lamp and (2) that the equipment may be cumbersome, heavy and difficult to store or transport. When the source of light generates considerable heat suitable provision must be made for ventilation.

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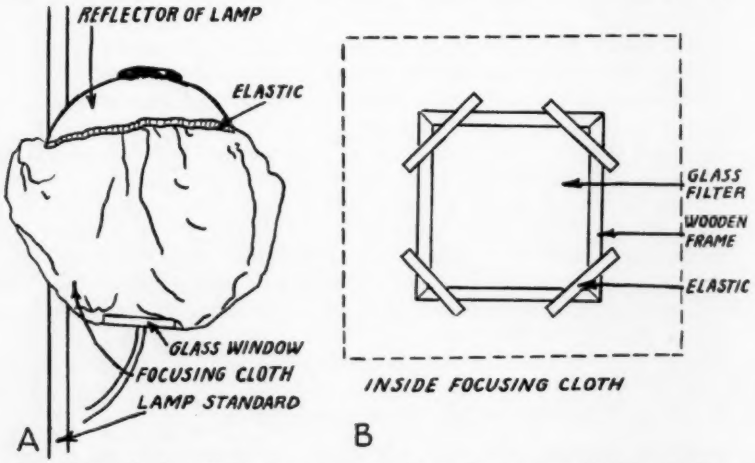
9. Davidson, A. M., and Gregory, P. H.: A Convenient Source of Wood's Light for the Diagnosis of Ringworm of the Scalp, Canad. M. A. J. **27**:176, 1932. Davidson, A. M.; Boyd, S. A., and Haltalin, C. P.: An Improved Source of Ultraviolet Light for the Diagnosis of Ringworm of the Scalp, Canad. M. A. J. **33**:534 (Nov.) 1935.

10. The Corning Glass Works, Corning, N. Y., furnishes violet ultra, no. 586, 6½ inches (16.51 cm.) square, polished on one side to a thickness of 4.5 mm., for $4.75; carrying charges are extra.

11. Mr. Harry Ashmore, an engineer, made a satisfactory attachment of this type for us.

OUR METHOD

The unit herewith described is light, easily attached and detached and readily stored, and it has proved durable in our hands. Any of the better makes of lamp for the production of ultraviolet rays may be used as a source of light. The material needed for the construction of the attachment is 1 square yard of light-proof black rubberized focusing cloth (obtainable at a camera shop). A hole 5 inches (12.5 cm.) square or smaller[12] is cut near the center of the cloth. The edges of the hole are hemmed. Then the glass filter is placed over this hole, overlapping the cloth on each side. Elastic loops are sewed diagonally across the four corners to hold the glass in place. If the fit is snug no light will seep around the edge of the glass. A hem is sewed around the edge of the cloth, in which is placed an elastic draw string. The cloth is then held up to and placed around the hood of an ultraviolet lamp, and the elastic draw string is tightened until the fit is close enough to exclude visible rays (fig. *A*). The ends of the draw string may then be sewed together so that later the cloth may be quickly



A, authors' device attached to an office lamp for the production of ultraviolet rays; *B*, inner aspect of the device, showing method of attachment of glass filter to the focusing cloth.

stretched around the hood of the lamp. In order to protect the glass filter from breakage a wooden frame may be glued to its edges (fig. *B*). When lamps that produce considerable heat are used the cloth may not wear well because of its rubber content. This objection does not arise when a better make of lamp is used. The approximate cost of the attachment (with 6½ inch [16.51 cm.] square filter) is $5.50.

SUMMARY

The important uses of filtered ultraviolet rays in dermatologic practice are enumerated.

An inexpensive, easily constructed unit for the isolation of rays of the correct wave lengths with which satisfactory fluorescence may be obtained is herewith described.

200 West Fifty-Ninth Street.

12. The size of the hole depends on the size of the glass filter. It is suggested that a hole 5 inches (12.5 cm.) square be used when the glass filter is 6½ inches (16.5 cm.) square.

Minor Notes

GLYCERIN AND BENZOIN LOTION

H. N. Cole, M.D., and Torald Sollmann, M.D., Cleveland

There is a real need for an inexpensive, practical hand lotion. A lotion, to be satisfactory, should make the skin soft, should not be too drying and should be easily applied. It is even better if, in addition to possessing these qualities, the lotion can be easily prepared.

Benzoin has been used a great deal in preparing hand lotions. One method of preparation has consisted in putting a few drops of tincture of benzoin in glycerin and rose water. However, the resin of the benzoin, which is insoluble in the mixture, had a tendency to separate as a milky emulsion or to form a sticky mass.

Another method has consisted in inserting a bag of gauze containing benzoin into heated glycerin and then adding the rose water. In this way a little of the benzoin was absorbed, but that method too has been unsuccessful.

A greatly superior hand lotion, which we have employed for years and which we have found to answer all the requirements is obtained by the use of a formula furnished by one of us (Dr. Sollmann). The method of preparation consists essentially in macerating benzoin (Siam benzoin) (3 per cent) in a mixture of glycerin and alcohol (3:1 by volume). The addition of the alcohol is the important feature of the process; it secures a better solution of the benzoin, and it "cuts" the viscosity of the glycerin, so that it spreads easily on the skin, leaving a thin layer when the alcohol has evaporated. The working formula is as follows:

Glycerin	640 cc.
Alcohol	240 cc.
Perfume (white lilac)	10 cc.
Water	80 cc.
Mix thoroughly and add Siam benzoin	30 Gm.

Siam benzoin makes a better lotion than the ordinary benzoin used commercially. The preparation is allowed to age for at least a week, but best results will be achieved if it is allowed to stand for from four to six months; thereafter the preparation may be decanted as necessary for use. It makes a perfectly clear, light yellowish liquid, pleasantly though not too strongly perfumed. The lotion is employed after washing and drying the hands. It is necessary to warn the user to employ only 2 or 3 drops. If a large amount is used the lotion is sticky; on the other hand, if only a small amount is employed, the skin is kept delightfully soft and free from cracking and scaling. The lotion is of practical use for physicians, dentists, housewives and other persons who must frequently wash the hands.

1352 Hanna Building.

PRESERVATION OF FUNGUS COLONIES BY FORMALDEHYDE

GEORGE M. LEWIS, M.D., AND MARY E. HOPPER, M.S., NEW YORK

An unwanted alteration in the appearance of many pathogenic fungi in culture referred to as pleomorphism[1] or monomorphism[2] may be retarded by keeping the fungus colony in a refrigerator or by transferring it to a growth-retarding medium. It may be impossible, however, to prevent the transition from occurring eventually. When the change occurs, a colony loses its typical appearance and may not be identifiable by its gross characteristics. Furthermore, it may be impossible in subsequent transfers to recapture the appearance of the original growth, and its identity may be permanently lost. Colonies of rare species of fungi, particularly, may not be in the best condition when they are needed for teaching purposes. By the method here described a fungus colony may be preserved in its typical form for an indefinite period. The gross appearance of the colony will remain unchanged for many months. The appearance under filtered ultraviolet rays,[3] however, changes to a noncharacteristic, dull color as soon as the growth is killed. A further advantage is that in keeping a virulent pathogen, such as Coccidioides immitis, for display purposes all danger of accidental human inoculation is eliminated.

METHOD

When a fungus colony has accquired a characteristic appearance, the cotton pledget is moistened by being dipped in a 40 per cent solution of formaldehyde and then replaced in the test tube. The growth is killed within twenty-four hours. The opening in the test tube should then be stoppered with a cork, or the cotton pledget may be dipped in paraffin so as to make a completely air-tight seal. This precaution is necessary to prevent evaporation of moisture from the agar with a resultant shriveling of the fungus growth.

SUMMARY

It is possible by the method here described to collect a permanent instructive exhibit of pathogenic fungi in culture.

200 West Fifty-Ninth Street.

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, George M. MacKee, M.D., Director.

1. Sabouraud, R.: Les teignes, Paris, Masson & Cie, 1910.
2. Fox, H.: Some Fungous Infections of the Skin and Appendages, Atlantic M. J. **30**:273 (Feb.) 1927.
3. Lewis, G. M.: Fluorescence of Fungus Colonies with Filtered Ultraviolet Radiation (Wood's Filter), Arch. Dermat. & Syph. **31**:329 (March) 1935.

HERPES ZOSTER WITH PARALYSIS OF ONE SIDE OF THE FACE

ARTHUR G. SCHOCH, M.D., DALLAS, TEXAS

Because paralysis of one side of the face is an infrequent complication of herpes zoster involving the superficial cervical plexus and because of the prompt favorable response to treatment with solution of posterior pituitary U. S. P. this report is made.

REPORT OF A CASE

H. L. P., a man aged 26, single, was seen on July 19, 1935, with lesions of herpes zoster involving the right side of the neck below the mandible, the lobe of the right ear and the right mastoid region. The duration of the eruption was five days. There were several enlarged, tender lymph nodes behind the angle of the right mandible. Seven groups of herpetic lesions were present.

There was complete paralysis of the right side of the face which had been present for only one day.

The patient was given 1 cc. of solution of posterior pituitary U. S. P. hypodermatically on the first, second and fourth days.

Symptomatic improvement was noted after the second injection, and ten days after the last treatment both the herpetic lesions and the paralysis of the right side of the face had completely disappeared.

COMMENT

The peripherial nerves involved were apparently the great auricular nerve and the cervical nerves in the skin. These nerves originate from the cervical plexus (second, third and fourth cervical nerve roots). A branch of the great auricular nerves communicates with the seventh nerve after that nerve leaves the stylomastoid foramen before dividing to supply the muscles of the face. A lesion at this site, an infectious neuritis, would explain the clinical picture in this case. An infection limited to the nuclei of the posterior nerve roots of the second and third cervical nerves would not explain the facial paralysis.

Furthermore, the facial paralysis was complete and hence peripheral; it was probably due to edema without destruction of the nerve fiber, otherwise complete recovery from facial paralysis in fourteen days could not have occurred.

1717 Pacific Avenue.

News and Comment

PROGRAM NOTICE, ATLANTIC CITY MEETING OF AMERICAN MEDICAL ASSOCIATION

Applicants for a place on the program of the Section on Dermatology and Syphilology of the American Medical Association at the meeting in Atlantic City, N. J., from June 7 to 11, 1937, are requested to submit titles and provisional abstracts of their proposed papers to the secretary of the section, Dr. Bedford Shelmire, Medical Arts Building, Dallas, Texas.

Applicants need not be members of this section but must be Fellows of the Association, graduates in medicine not in private practice or invited guests.

PERSONAL

In the July issue of the ARCHIVES it was announced that Dr. Mihran B. Parounagian had resigned his position as visiting dermatologist and syphilologist to Bellevue Hospital on account of ill health. Fortunately, Dr. Parounagian has recovered and is again active in private practice.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

ROENTGEN-POSITIVE SERONEGATIVE INFANTILE CONGENITAL SYPHILIS. NORMAN R. INGRAHAM JR., Am. J. Dis. Child. **50**:1444 (Dec.) 1935.

Ingraham states that in the year from Jan. 1 to Dec. 31, 1934, at the Philadelphia General Hospital, though the incidence of syphilis among the pregnant women was 11.8 per cent and the majority of the patients received insufficient prenatal antisyphilitic therapy to insure the birth of healthy children, not one of the 1,517 babies discharged alive from the maternity division showed any clinical evidence of congenital syphilis. The Wassermann reaction was of value in diagnosing syphilis in not more than 9 syphilitic children among 195 offspring of syphilitic mothers. The roentgenogram discovered 40 additional cases, 26 (19.4 per cent) being recognized before the patient was 6 days old and 23 cases (17.1 per cent), when the patient was from 1 to 10 months old. In all these cases the initial skeletal changes were evident roentgenographically before the blood serum gave a positive reaction.

Treatment of the mother before delivery affects the early roentgenographic evidence as follows: Of 51 cases in which the mothers were treated more than two months, in 5 (9.8 per cent) syphilis was shown in the infants roentgenographically at 6 days; of 68 cases in which the mothers were treated less than two months, in 21 (30.8 per cent) there was positive roentgenographic evidence of syphilis in the offspring. Cases in which the roentgenograms revealed no positive signs at the age of 6 days were studied at ages from 3 to 6 months. Of 36 cases adequately followed, in 12 (33 per cent) the roentgenographic evidence subsequently became positive.

In 3 cases serial roentgenograms of the same child taken over a period of several months are shown, leaving no reasonable doubt that the earlier changes in the bones seen a few days after birth are the precursors of the more advanced and easily recognized osseous lesions which developed subsequently. The Wassermann reaction which originally was negative became positive as the disease progressed, making a syphilitic etiology seem certain. AUTHOR'S SUMMARY.

KAPOSI'S VARICELLIFORM ERUPTION. EDWARD F. CORSON and JOHN B. LUDY, Am. J. Dis. Child. **50**:1476 (Dec.) 1935.

Corson and Ludy report three cases of Kaposi's varicelliform eruption, two occurring in infants and one in a boy 9 years of age. The three patients had suffered from a previous eczema. The eruption resembled variola a great deal more than varicella. The lesions were umbilicated pustules of quite uniform size. Constitutional symptoms associated with fever and malaise were present. Healing occurred without scarring. The authors state that previous vaccination for smallpox and bullous erythema multiforme must be considered in the differential diagnosis. The areas involved are the face, neck, hands, wrists and forearms.

SUCCESSFUL TREATMENT OF NOMA WITH FORMALDEHYDE. S. I. MCMILLEN, Am. J. Dis. Child. **50**:1495 (Dec.) 1935.

McMillen reports two cases of noma (gangrenous stomatitis). In one case treatment with fuming nitric acid was of no avail. In the other case after fuming nitric acid had failed to stop the spread of the disease, undiluted formaldehyde (British Pharmacopeia) was applied once daily for five days, and an exceedingly satisfactory result followed.

THE INFLUENCE OF INADEQUATE TREATMENT OF EARLY SYPHILIS ON THE INCIDENCE AND INCUBATION PERIOD OF NEUROSYPHILIS. J. E. KEMP and W. C. MENNINGER, Bull. Johns Hopkins Hosp. **58**:24 (Jan.) 1936.

This study was made to test the validity of the assumption that inadequate treatment of early syphilis not only increases the incidence of neurosyphilis but shortens the interval between infection and the appearance of clinical evidence of neurologic damage. In a study of 680 patients, 265 of whom had neurosyphilis, Kemp and Menninger made the following observations: 1. Inadequate treatment given early (within two years after infection) apparently does not increase the incidence of neurosyphilis. When no treatment was given the percentage of cases of neurosyphilis was 52.6, and when inadequate treatment was given early it was 43.4.

2. The incidence of neurosyphilis in male patients given no treatment and in those given inadequate treatment was 57.4 and 57 per cent, respectively. In female patients the incidence in the group given inadequate treatment was 32.2 per cent, and in the group given no treatment, 50 per cent. Thus, by comparison of the incidence in a group without treatment, it appears that in females inadequate treatment given early reduces the incidence of neurosyphilis.

3. The incubation period of clinical neurosyphilis was reduced approximately five years in a group of patients who received inadequate treatment early in the disease as compared with a group receiving no treatment; i. e., it was reduced from nineteen and two-tenths to thirteen and one-tenth years in males and from fourteen and nine-tenths to eight and seven-tenths years in females.

4. The incubation period of neurosyphilis was shorter in females than in males both in the treated and in the untreated group. The reason for this difference is not apparent from this study. NELSON PAUL ANDERSON, Los Angeles.

SENSITIVITY TO INGESTED YEAST. J. B. BIEDERMAN, J. A. M. A. **106**:31 (Jan. 4) 1936.

Ingested yeast was found by Biederman to be responsible for allergic diseases in four patients. The response to the allergin differed in each patient, producing asthma in the first patient, eczema in the second, hay fever in the third and urticaria and angioneurotic edema in the fourth. Confirmation in each case was established by positive cutaneous reactions to tests with yeast and by the return of symptoms after ingestion of yeast when its withdrawal from the diet had resulted in a disappearance of the allergic response. Biederman suggests that tests with yeast be included in routine cutaneous tests.

RECOMMENDATIONS FOR A VENEREAL DISEASE CONTROL PROGRAM IN STATE AND LOCAL HEALTH DEPARTMENTS: SUMMARY REPORT OF AN ADVISORY COMMITTEE TO THE U. S. PUBLIC HEALTH SERVICE. R. A. VONDERLEHR and others, J. A. M. A. **106**:115 (Jan. 11) 1936.

In a report by an advisory committee to the United States Public Health Service, a broad and comprehensive program to control venereal disease was outlined. The following points were emphasized: The organization of the program should be in the hands of a full time officer, who should have a local advisory committee. Adequate funds should be available to provide requisite facilities for treatment of indigent patients and to take care of emergencies. In rural districts, subsidies to counties and communities might be required to transport patients to the nearest center of treatment. In each state at least one or two centers for diagnosis and treatment of venereal diseases should be established in which, among the other services, roentgen and other special laboratory facilities should be provided. Such centers should be consultant in nature. To prevent hereditary syphilis, a blood test should be made of every pregnant woman, and when the test is positive, antisyphilitic treatment should be given. Follow-up or epidemiologic investigation of each infectious case and also of cases in which lapse from treat-

ment has occurred is considered essential. Adequate laboratory facilities should exist; emphasis should be laid on dark-field examinations and lumbar punctures. The health departments should cooperate with private physicians by providing free diagnostic service and free antisyphilitic drugs when the patient is a menace to public health and by making consultation services available. The collection of adequate morbidity and mortality reports should constitute an important function of the officer in charge. Informative literature should be disseminated among physicians, nurses and other workers. Undergraduate and postgraduate training should stress the efficient handling of venereal diseases. Educational material should be disseminated among the general public.

TORULOSIS. LOUIS A. MITCHELL, J. A. M. A. **106**:450 (Feb. 8) 1936.

The patient whose case is reported contracted the disease two weeks before he was first observed. He complained of frontal headache, weakness and dizziness. He was also nauseated and vomited frequently. His mental state was stuporous, and he was quite restless, excitable and apprehensive. There were marked photophobia and nystagmus; the muscles of the neck were spastic, and the patellar reflexes were absent. The hemoglobin content was 50 per cent; the total leukocytes numbered 7,000, and there were 95 per cent polymorphonuclears. The spinal fluid was cloudy and was under high tension. Mycologic examinations revealed heavy walled, round bodies with buds. Gram stain showed gram-positive budding yeast-like bodies. An india ink preparation revealed a wide capsule. The average diameter of the organism was 21 microns. The organism was grown on several different mediums. Fermentation tests gave negative results. Mitchell also comments on the literature, pointing out that various internal organs and the skin may be infected with this organism. The infection is of low pathogenicity until the central nervous system is invaded, at which time the clinical course becomes fairly rapidly fatal. The association of torulosis and Hodgkin's disease appears to be more frequent than could be accounted for by the theory of probability.

COOPERATIVE CLINICAL STUDIES IN THE TREATMENT OF SYPHILIS: SYPHILIS IN PREGNANCY. HAROLD N. COLE and others, J. A. M. A. **106**:464 (Feb. 8) 1936.

It was shown that even inadequate antisyphilitic treatment administered during pregnancy is of value to the unborn child. The desideratum is continuous treatment during the entire period of each pregnancy for any syphilitic patient, and it is particularly desirable that treatment be administered before the fifth month of the pregnancy. In cases in which early stages of syphilis developed late in the pregnancy, treatment until the termination of the pregnancy proved to be of value. In only 7.6 per cent of the cases in which treatment for early stages of syphilis was given after the fifth month of the pregnancy were the children born dead, whereas in control cases in which no treatment was administered the incidence of stillbirths was 46 per cent. Pregnant syphilitic women were found to tolerate antisyphilitic treatment as well as, or better than, syphilitic women who had not been pregnant since they contracted the infection. LEWIS, New York.

ORAL DESENSITIZATION TO COMMON FOODS. BEATRICE M. KESTON, IRENE WATERS and J. GARDNER HOPKINS, J. Allergy **6**:431 (July) 1935.

The method of making dilutions of the more common foods is given. The first dilution is calculated to make the initial dose contain 1 mg. of protein. The dose is increased every four days. If symptoms recur the dose is decreased to that of twelve or sixteen days previous. If the symptoms continue the desensitization is discontinued until they subside.

The method has been used successively for five years in desensitizing persons sensitive to the common foods, especially children with chronic allergic eczema.

Any one interested in this subject should send to the authors for a reprint. It is said to contain lists of foods to be avoided during desensitization. These lists are omitted from the article because of their length.

HOYER, Cincinnati. [AM. J. DIS. CHILD.]

THE EFFECT OF THE ANGLE OF INCIDENCE UPON THE DOSE OF X-RAYS ABSORBED BY THE SKIN. E. H. MOLESWORTH and A. R. RIDDLE, Brit. J. Dermat. **47**:152 (April) 1935.

Molesworth and Riddle show that the angle of incidence of a beam of roentgen rays has little or no influence on the dose actually absorbed in tissues immediately below the surface irradiated. They arrived at this conclusion by mathematical calculations and by the use of a photographic film. Two strips of a photographic film were used. One strip was put in a plane normal to the beam of roentgen rays, and the other was tilted at an angle of 45 degrees. The strips were exposed under uniform conditions and developed in the same tank at the same time. The amount of clouding noted in both strips was the same. Therefore it was proved that the amount of roentgen rays absorbed is not dependent on the angle of incidence but on the energy applied (intensity).

In applying this knowledge to irradiation of the scalp in cases of tinea tonsurans, the authors found that when the five point irradiation according to the method of Adamson and Kienböck was used the areas between the centers of irradiation received an amount of roentgen irradiation far in excess of that applied at the centers. The increased dose in the areas of overlap is dependent on the focal skin distance. Calculations based on the law that the intensity varies inversely as the square of the distance show that the use of any focal skin distance greater than 8.5 cm. causes an overdose in the region of overlap. This distance is impractical because it brings the head too close to the tube and because only the middle third of two adjacent centers receives overlapping irradiation. Complete overlapping is necessary to achieve even distribution of dose, and in order to obtain this the focal skin distance must be increased.

Molesworth and Riddle make the following statement:

"If a system of irradiating can be evolved so that the disparity of dose distribution is considerably reduced, the margin of safety should be wide enough to permit the performance of x-ray epilation with almost complete safety in all cases."

[I have suspected for several years that an overdose of roentgen rays was applied to the areas between centers of irradiation in the five point technic of Adamson and Kienböck for epilating the scalp. I never carried out experiments to prove or disprove this theory. The mathematical and physical calculations of Molesworth and Riddle conclusively show that an overdose occurs in the areas of overlap and that the amount of irradiation absorbed by a few millimeters of tissue is independent of the angle of incidence. The point mentioned by the authors and the fact which should be emphasized is that the margin between the smallest dose that will cause epilation and the largest dose which will fail to prevent regrowth must be much greater than has been believed hitherto.

The technic of Adamson and Kienböck has been used successfully for many years. I believe that until a practical technic is evolved which will overcome the objections raised by Molesworth and Riddle it is safer to adhere to the technic described by MacKee in his book. Abstractor.] CIPOLLARO, New York.

DEFINITION AND ETIOLOGY OF ECZEMA. JOHN T. INGRAM, Brit. J. Dermat. **47**:502 (Dec.) 1935.

Ingram expresses the belief that the essential characteristic of eczema is the fact that it is an itching, uniform, pinhead-sized eruption. This reaction is seen both clinically and histologically. The etiology depends on hypersensitiveness of the skin, an external irritant and autosensitization. The hypersensitiveness of the skin is part of the physiologic instability of the patient and may be inborn

or result from temporary circumstances. A state of nervous instability, malnutrition, an abnormal metabolic state or a toxic state acting locally or generally may occasion the physiologic instability.

The external factor may be any stimulus. In addition there is the factor of autosensitization of the patient to the serum of his own exudates. If the serum is in contact with the skin, an external eruption results. If the serum is reabsorbed into the blood, a generalized eruption may result. Seven illustrations are given.

PANNICULITIS: ITS PLACE IN NOSOLOGY. H. KEIL, Brit. J. Dermat. **47**:512 (Dec.) 1935.

According to Keil, the name "primary panniculitis" refers to the condition in which changes occur in the adipose tissue over wide stretches of the body but no suppuration is present. There are two forms of the condition: the febrile and the afebrile. The febrile form is characterized by croplike outbreaks of slightly tender subcutaneous nodules on the extremities associated with prolonged irregular fever and constitutional symptoms. The nodules involute, leaving atrophy of the adipose tissue and dimpling of the skin. Cultures of the blood are sterile. The afebrile form is characterized by massive, painless induration of the subcutaneous tissues of the anterior aspect of the trunk, the overlying skin remaining uninvolved.

Keil states that secondary panniculitis may occur coincidentally with erythema nodosum, nodular erythema due to a drug, erythema induratum, Darier-Roussy's sarcoid, lipogranuloma and dermatomyositis (?).

A CASE OF PARAFFINOMA. MASON BOLAM, Brit. J. Dermat. **47**:523 (Dec.) 1935.

Bolam reports the clinical and histologic observations in a case of paraffinoma occurring in a man aged 36. Lesions occurred on the arms, on the calf of both legs and in the left iliac region at the sites where some drug had been injected nine years before.

The histologic examination revealed a chronic panniculitis without change in the elastic tissue and multiple oil cysts filled with a material which was not double refracting.

Bolam expresses the belief that these nodules may be due to impurities in the substance injected or to a personal susceptibility of the patient to that substance. A brief review of the literature and a photomicrograph are given.

WIEN, Chicago.

STUDIES ON INFANTILE ACRODYNIA: I. NOTE ON THE YEARLY AND SEASONAL INCIDENCE. E. LEENHARDT and J. BOUCOMONT, Rev. franç. de pédiat. **11**:265, 1935.

In the course of the last seven years the authors have observed thirty-eight cases of acrodynia. The number has increased yearly, and in 1934 fifteen cases were observed. By far the greatest number occurred in the winter and spring. The authors raise the question as to whether acrodynia is a neurovegetative localization of a banal infection of the respiratory passages. They also cite the hypothesis of Moro that there is hyperexcitability of the vegetative nervous system in the spring, which in certain infants may take the form of acrodynia.

LESLIE, Evanston, Ill. [AM. J. DIS. CHILD.]

CUTANEOCEREBRAL ANGIOMA. J. S. CHARAMIS, Rev. d'oto-neuro-opht. **12**:755 (Dec.) 1934.

Certain cutaneous vascular lesions, such as vascular nevi of the face, may be accompanied by true cerebral angioma. Often they are accompanied by angioma of the retina. These disorders must not be confused with angiogliomatosis of the retina, with atypical Recklinghausen's disease associated with cerebral lesions,

or with pure cerebral angioma without any cutaneous or ocular lesions. A boy, aged 14, presented mucocutaneous angiomatous nevi in the region supplied by the right trigeminal nerve, with homolateral cerebral angioma; there were no signs of a pathologic neurologic process except epileptic attacks and mental dulness, but pronounced calcification of the vascular tumor, syphilitic iridocyclitis in the right eye, and positive reactions to the Wassermann and Hecht tests were present. While the pathogenesis in these cases is not settled, Charamis is inclined to attribute the cause of the diseases in this case to syphilis. Active antisyphilitic treatment and high voltage roentgen therapy were applied. If the cerebral complications become menacing, extirpation of the tumor is indicated, in spite of the attendant risks. DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

BLASTOMYCOSIS DUE TO SCOPULARIOPSIS BREVICAULIS. LUIGI CIARROCCHI, Gior. ital. di dermat. e sif. **76**:1409 (Dec.) 1935.

Ciarrocchi reports a case of dermatitis circumscribed to the upper third of the right forearm occurring in a man aged 29. Scopulariopsis brevicaulis var. hominis (Brumpt and Langeron) was recovered. The patient had an uneventful recovery as a result of treatment with a salve containing salicylic acid and sulfur. Intradermal tests with fungus extract were positive, and agglutinins were present in the blood serum of the patient. Inoculation of animals gave negative results.

SEASONAL VESICOBULLOUS DERMATITIS PRODUCED BY A BEETLE (PAEDERUS FUSCIPES, FAM. STAPHYLINIDAE). A. BACCAREDDA, Gior. ital. di dermat. e sif. **76**:1423 (Dec.) 1935.

Baccaredda identified a small beetle (Paederus fuscipes) as the cause of a recurrent seasonal vesicobullous dermatitis occurring in small epidemics during the summer and affecting the uncovered parts, especially the face and neck. A similar dermatitis due to a member of the species "fuscipes" has been described as occurring in southern Russia. PARDO-CASTELLO, Havana, Cuba.

A SIMPLE METHOD FOR THE REMOVAL OF TATTOOING. JANSON, Dermat. Wchnschr. **101**:894 (July 20) 1935.

Janson states that in 1921 he observed that soldiers living in relatively unsanitary surroundings exhibited folliculitis and excoriations from scratching. In several instances he noted the disappearance of tattooing in areas which had been subjected to constant scratching and secondary infection. Subsequently he removed a tatoo from a patient's back by scrubbing the area with a stiff bristled brush, the area being anesthetized with procaine hydrochloride. Three treatments resulted in the disappearance of the tattoo, and according to the author, the cosmetic effect was very good "for a man's back."

EXCRETION OF SODIUM CHLORIDE IN FEBRILE PATIENTS AND ITS IMPORTANCE IN REGARD TO THE SO-CALLED SALT RETENTION IN PATIENTS WITH PEMPHIGUS VULGARIS. HUGO WOLFF, Dermat. Wchnschr. **101**:911 (July 27) 1935.

From a series of tests of the sodium chloride metabolism, Wolff draws the following conclusions: 1. All toxic febrile patients show a decrease in urinary excretion of sodium chloride. This may be interpreted as a retention of the salt but it is balanced by increased excretion of sodium chloride in the sweat. 2. In patients with a high fever and marked sweating sodium chloride may be entirely absent from the urine. 3. Artificially produced fever causes the same decrease in the salt content of the urine. 4. The length of time before excretion of salt in the urine returns to normal depends on the height and duration of the fever.

Wolff concludes that it is evident that the frequently reported retention of salt in patients with pemphigus is only apparent.

LEUKODERMA FOLLOWING A LATE RECURRENT SYPHILITIC EXANTHEM. THOMAS PREININGER, Dermat. Wchnschr. **101**:916 (July 27) 1935.

Depigmented areas developed on the chest, the labia pudendi and in the intergluteal cleft of a patient with resistant recurring syphilis.

OSTEITIS TUBERCULOSA MULTIPLEX CYSTOIDES (JÜNGLING) IN A CASE OF LUPUS VULGARIS. FRANZ KOCH, Dermat. Wchnschr. **101**:919 (July 27) 1935.

A case of typical lupus vulgaris associated with osteitis tuberculosa multiplex cystoides is described. Injections of tuberculin produced a flare-up of the cutaneous condition and also pains in the fingers affected by the osteitis.

TO WHAT EXTENT DOES THE NECESSARY DURATION OF ANTISYPHILITIC THERAPY DEPEND ON ITS INTENSITY? E. ZURHELLE, Dermat. Ztschr. **72**:57 (Sept.) 1935.

Zurhelle has had experience with the short intensive courses of antisyphilitic treatment advocated in Bonn, Germany, and with the longer less intensive courses formerly used in Groningen, Netherlands. He states that the shorter, more intensive courses are as effective, a lower total amount of arsphenamine and bismuth being administered. He therefore makes use of the "maximal treatment" whenever this is practicable. Toxic effects from the medication were no more frequent in patients receiving the intensive than in those receiving the longer courses of treatment.

EROSIVE PLURI-ORIFICIAL ECTODERMOSIS AND ITS RELATION TO ERYTHEMA EXSUDATIVUM MULTIFORME. L. KUMER, Dermat. Ztschr. **72**:62 (Sept.) 1935.

Under the name erosive pluri-orificial ectodermosis French authors have described an acute febrile disease characterized by the formation of bullae and vesicles on the buccal mucosa and of pseudomembranes. Other mucous membranes are often involved. Cutaneous eruptions in the form of papules, bullae, purpuric or varicelliform lesions are frequently seen. Recurrences occur in most instances. Kumer describes two cases of a disorder that apparently belongs in this classification. He expresses the belief that the dermatostomatitis described by Baader is the same condition and that in both instances the disorder may have been an atypical manifestation of erythema multiforme.

NEW CLINICAL AND EXPERIMENTAL CONTRIBUTIONS TO THE QUESTION OF LYMPHOGRANULOMA VENEREUM. H. LÖHE and H. SCHLOSSBERGER, Dermat. Ztschr. **72**:70 (Sept.) 1935.

Material obtained from a patient with lymphogranuloma venereum was injected into monkeys and guinea-pigs. The infection was carried through a number of generations, and this passage markedly increased the virulence of the virus. Filtration through a Seitz filter caused a considerable decrease in the virulence.

TAUSSIG, San Francisco.

CUTANEOUS METASTASES IN THE FIELD OF IRRADIATION OF A PYLORIC CANCER. O. SCHÜRCH, Ztschr. f. Krebsforsch. **41**:47, 1934.

There is described a case of pyloric carcinoma in which after operation (without excision) and prophylactic irradiation early cutaneous metastases appeared which were limited to the irradiated area. The phenomenon is directly the opposite of what would be expected from experimental observations. Schürch explains it on the ground of vascular trauma by the irradiation, with establishment of a site of lowered local resistance to tumor implantation.

EGGERS, Omaha. [ARCH. PATH.]

CONTRIBUTION TO EXPERIMENTAL SPOROTRICHOSIS: I. EXPERIMENTAL INOCULATIONS OF SPOROTRICHUM BEURMANNI (KOBAYASI STRAIN) INTO WHITE RATS AND RABBITS. T. KOBAYASI, Jap. J. Dermat. & Urol. **38**:747 (Nov.) 1935.

Kobayasi reports experimental work on sporotrichosis caused by inoculation of white rats and rabbits with Sporotrichum Beurmanni (Kobayasi strain). The clinical observations were reported previously (*Jap. J. Dermat. & Urol.* **36**:665, 1934) and abstracted in the ARCHIVES (**37**:648 [Oct.] 1935). Another report (*Nagasaki Igakkai Zassi* **13**:1687 [Nov.] 1935) is not available at present.

The infective material was inoculated subcutaneously, intravenously into the marginal vein of the ear of rabbits and intraperitoneally. The subcutaneous inoculations resulted in a local abscess consisting histologically of a small central abscess surrounded by a rather narrow middle layer consisting chiefly of histiogenic wandering cells or histiocytes of Kiyono (possibly plasma cells) and by an outer layer consisting chiefly of a fibroblastic reaction (granulation tissue).

The intravenous inoculations resulted in so-called sporotrichotic pneumonia, or pulmonary sporotrichosis. This process consisted in the main of initial sporotrichotic embolism (miliary sporotrichotic tubercles) and later caseous pneumonia or pulmonary hepatization. The early embolic lesion consisted of an initial infiltration of the intravascular embolus and surrounding tissues with histiocytes, which later assumed an epithelioid character, and of an outer layer of connective tissue reaction. A few giant cells were intermixed, particularly in the outer zones, and the majority contained fungous bodies and cellular débris and were evidently foreign body giant cells. Yet a few of them did not have inclusions and histologically appeared to be typical Langhans giant cells.

Because of a mistake the intraperitoneal inoculations resulted in some cases in retroperitoneal inoculations, causing a perinephric abscess and pulmonary metastases as described; in other cases the intraperitoneal inoculations were successful and caused an initial intense peritoneal reaction (leukocytic extravasation) and later resorption, intraperitoneal walling off or so-called milkspot (Langerhans' *Trübung*) followed in some instances by eventual resorption. The pathogenic fungus was obtained by culture of material from the lesions and, in the case of animals with metastatic perinephric abscesses, from the heart blood.

In all the lesions the pathogenic fungus could be seen microscopically as a small deeply stained round or oval body with a strongly refractive capsule, measuring from 2 to 3 microns in diameter.

ECZEMATOUS CHANGES IN THE SKIN AND FAT METABOLISM. T. OZAKI, Jap. J. Dermat. & Urol. **38**:771 (Nov.) 1935.

Ozaki studied the total fatty acids, phosphatides (lecithin) and total cholesterol content of the skin in relation to experimental dermatitis produced by croton oil. The total fatty acids were extracted with ether and alcohol, saponified with sodium hydroxide and weighed dry. The phosphorus content of the lecithin substances, ashed with sulfuric acid and fuming nitric acid, was determined by multiplying the theoretical factor 0.054 by the amount of four hundredths-normal sodium hydroxide required to dissolve a precipitate of ammonium phosphomolybdenate. For determination of the cholesterol content the free cholesterol was weighed as a digitonin precipitate, the residual cholesterol ester being then saponified with sodium alcoholate and precipitated and weighed as described for phosphorus. The methods used are those described in Takata's "Biochemical Analysis" (Shōkwagaki Bunseki, 1927, p. 610), the digitonin method being a modification of the Windaus method (*Ztschr. f. physiol. Chem.* **65**:110, 1910).

During the acute stage of the croton oil dermatitis in the rabbit the amounts of total fatty acids, phosphatides and cholesterol diminish markedly; they rise to abnormally high values during the subacute stage (nineteenth day) and finally sink gradually back to normal. Tables showing the variations of each constituent in milligrams per hundred grams of skin accompany the article.

The conclusion is that experimental dermatitis exerts an influence on the metabolism of fats.

J. W. BRENNAN, Chicago.

CASE OF ERYTHEMA ANNULARE (LEHNDORFF AND LEINER). J. A. VAN KRIEKEN, Maandschr. v. kindergeneesk. **4**:224 (March) 1935.

A description is given of a case of the erythema annulare of Lehndorff and Leiner in a girl, aged 7 years, who was admitted to the hospital for the treatment of gonorrheal vulvovaginitis. During her stay in the hospital acute rheumatic fever developed, associated with rheumatic endocarditis and annular erythema.

ONE HUNDRED AND TWENTY CASES OF ERYTHEMA NODOSUM. H. SANDRA, Nederl. tijdschr. v. geneesk. **79**:13 (Jan. 15) 1935.

A detailed report is given of one hundred and twenty cases of erythema nodosum, in which examination was made at a consultation office for tuberculous patients. The number of adults was twice that of children. In accord with Wallgren and many other authors, erythema nodosum is considered in most cases to be a symptom of tuberculous infection. The early detection of all patients with erythema nodosum is of great importance for a successful fight against tuberculosis, and the consultation offices should be charged with this task.

HEREDITY OF ALBINISMUS CIRCUMSCRIPTUS. J. SANDERS, Nederl. tijdschr. v. geneesk. **79**:1245 (March 23) 1935.

Three families consisting of seventy-four persons are described, in thirty-nine of whom albinismus circumscriptus occurred on the forehead, abdomen and legs. The anomaly is dominant. The hypothesis of Frassetto regarding the cause of this hereditary deviation is discussed. In the author's opinion, this hypothesis cannot explain the occurrence in all the cases.

PSORIASIS AND MEASLES. C. H. BEEK, Nederl. tijdschr. v. geneesk. **79**:4157 (Aug. 31) 1935.

Through an investigation of the anamneses of 100 adults suffering from psoriasis and of 100 persons used as controls, it could be proved that in both groups there was a history of measles. This observation is contrary to the opinion that measles protects against psoriasis.

DERMATITIS GANGRAENOSA INFANTUM. I. COHEN, Nederl. tijdschr. v. geneesk. **79**:5143 (Nov. 2) 1935.

The description is given of a case of dermatitis gangraenosa in a baby 1 month old, who until ten days after birth had been healthy. In material obtained from a complicating closed cutaneous abscess only Staphylococcus aureus was observed. Notwithstanding the age, the progress of the ulcers and the serious general state of the child, recovery was obtained after two months' hospitalization, the most important therapeutic agents being numerous injections of antistaphylococcus serum and daily blood transfusions.

VAN CREVELD, Amsterdam, Netherlands. [AM. J. DIS. CHILD.]

Society Transactions

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. Driver, M.D., *Reporter*

Regular Meeting, Dec. 26, 1935

H. G. Miskjian, M.D., *Presiding*

Intracranial Hemangioma with Hemiplegia. Presented by Dr. John A. Gammel.

J. S., a boy aged 8 years, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, was born with port wine nevi involving the right half of the face and areas on the upper and lower extremities. At the age of 18 months he had a convulsion; this was followed by a spastic hemiplegia on the right side which has persisted, impairing the function of the leg and arm. The child is undersized, has a relatively large head and asymmetry of the face and is mentally underdeveloped. On the right side of the face, on the distal two thirds of the upper extremities and on the legs are areas of port wine nevi. There is marked bony and muscular atrophy of the right upper and of the lower extremities. When the patient walks he drags his right foot. There is generalized weakness of the entire right side. There is moderate ptosis of the right eyelid. The scleras of both eyes are bluish. The pupillary reflexes are normal; the tendon reflexes are present and are apparently normal on both sides in the arms and legs. The tongue protrudes in the midline.

The Wassermann reaction of the blood was negative. The blood cell count and differential counts were normal; the hemoglobin content of the blood was 73 per cent.

A roentgenogram of the skull made in November 1935 showed it to be asymmetrical, presenting a bulge in the right parietal region. There was evidence of thickening of the left parietal bone, which measured 15 mm. in thickness. The frontal and occipital bones were markedly thickened. The inner and outer contour of the bones of the skull appeared to be normal. The sutures were well visualized, and their ossification appeared to be normal. The sella turcica appeared to be normal. The sphenoid sinuses were not developed.

DISCUSSION

Dr. E. W. Netherton: I had occasion some time ago to look up the association of neurologic lesions with the presence of nevi. I was rather surprised to find that disorders such as the one in this child are not rare. There are cases reported in the pediatric literature. The condition is probably due to a vascular nevus involving the meninges, the hemiplegia being due to hemorrhage.

Cerebrospinal Syphilis (Syphilitic Amyotrophy). Presented by Dr. John A. Gammel and Dr. Paul G. Reque.

J. R., a Negro aged 53, from the outpatient department of the Lakeside Hospital, contracted syphilis in 1906 and received little or no antisyphilitic treatment. In March 1935 he was admitted to the Lakeside Hospital because of weakness in his hands of two years' duration. For several months this weakness had also been present in his legs. He complained of an aching sensation in the knees, hips and shoulder. During the past four months the weakness has become

progressively worse and has been associated with moderate stiffness of the elbow joints. The patient is well developed but rather poorly nourished. Marked muscular weakness is demonstrable in both the upper and the lower extremities. All the tendon reflexes are hyperactive. There is no demonstrable sensory disturbance and no ataxia. The Babinski sign is equivocal. Examination of the cranial nerves showed that all were intact. The patient has no difficulty of speech. The pupils are small and fixed to light but react slightly in accommodation. The eyegrounds are normal. There are no physical abnormalities. Urinalysis gave negative results. The blood cell count, the differential count and the hemoglobin content of the blood were normal. The Wassermann reaction of the blood was 2 plus. The spinal fluid was under 100 mm. of pressure. The Pandy reaction was negative; the number of cells in the spinal fluid was normal; the Wassermann reaction was 2 plus in 0.5 cc. and 4 plus in 1 cc. of fluid; the mastic curve was normal.

A roentgenogram revealed atrophic arthritis in the hands. There was a moderate amount of periostitis about the left elbow; a roentgenogram of the skull showed no abnormalities.

Treatment has consisted of intramuscular injections of thiobismol and bismuth and potassium tartrate and internal administration of potassium iodide. There has been no progress of the disease since treatment was started, but improvement, if any has occurred, has been slight.

DISCUSSION

DR. JOHN E. RAUSCHKOLB: In making a differential diagnosis one would have to consider, in addition to syphilis of the central nervous system, the possibility of an alcoholic peripheral neuritis or atrophy associated with pseudopellagra.

DR. W. H. CONNOR: Recently at the City Hospital there were two patients whose disorder could be classed in the same group as that of this man. Examinations of the spinal fluid gave results similar to those reported by Dr. Gammel and Dr. Reque. The response to antisyphilitic treatment has been poor.

DR. H. N. COLE: This type of syphilis of the central nervous system is rare and interesting. There is usually an involvement of the lateral columns of the spinal cord. The syndrome is fairly characteristic.

MACULAR ATROPHY OF THE SKIN. Presented by DR. H. G. MISKJIAN and DR. MAURICE SULLIVAN.

CASE 1.—L. M., a Negress aged 41, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, was first seen in the outpatient department in August 1935, when she complained of a large gumma of the skin of the left forearm, which had healed with scar formation after the institution of antisyphilitic treatment. It was noted at the time of the first examination that the patient had an extensive eruption, chiefly over the back, consisting of rounded atrophic lesions varying in size from that of a split pea to that of a bean. These lesions on palpation gave the impression of a circumscribed loss of elasticity of the skin. The duration of these lesions was indefinite. Biopsy of material from one of the atrophic lesions showed the thickness of the epidermis to be decreased. The papillary pegs were completely flattened. The total thickness of the corium was greatly decreased. There was undulation of swollen connective tissue fibers in the deeper portions. Cellular infiltration in the superior layer was sparse. Elastic tissue fibers were absent.

The Wassermann reaction of the blood was strongly positive. Examination of the spinal fluid gave negative results.

CASE 2.—P. S., a Negress aged 33, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, had a generalized eruption and some moist perianal sores in 1921. Tests of the blood made at that time gave strongly positive reactions. After antisyphilitic treatment was administered the lesions on the skin healed, leaving scars, which have persisted. Over the entire body but espe-

cially marked over the trunk are numerous round and oval atrophic lesions; they vary in size from 2 to 2.5 cm. in diameter, and few are even larger. Some of these lesions present a ballooned appearance, but on palpation they are soft, inelastic and atrophic.

Biopsy showed the epidermis to be flattened in the corium. The connective tissue is edematous. There is a moderate amount of round cell infiltration about the vessels. Elastic tissue fibers are absent.

CASE 3.—E. T., a woman aged 49, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital was admitted to the hospital in March 1935 for hemorrhoidectomy. On examination at that time it was noted that the patient had widely scattered atrophic lesions on the skin. She stated that these had been present for only a few months and that there had been no preexisting inflammatory eruption. On the arms, forearms and shoulders are a few widely scattered irregular and round raised and depressed lesions approximately 1 cm. in diameter. The lesions are bluish white and resemble bladder-like formations. On palpation they give the impression of small hernia-like lesions of the skin. The Wassermann reaction of the blood was negative. Biopsy showed a thin layer of stratified squamous epithelium with narrow bands of keratin on its surface. The rete pegs were small and flattened and in some areas were entirely absent. In the corium was dense hyalinized connective tissue with a scarcity of elastic fibers. There were small accumulations of mononuclear cells around the smaller vessels of the corium.

DISCUSSION

DR. BENJAMIN LEVINE: I was able to elicit a history of varicella in two of the cases; I believe that in these the atrophy is more or less typical of that which follows this disease and that it does not represent true macular atrophy. The condition in the other case, however, seems to be characteristic of syphilitic macular atrophy.

DR. H. J. PARKHURST, Toledo, Ohio: In the two Negro patients the macular atrophy following secondary syphilis seems quite apparent to me. The eruption exhibited by the third patient is characteristic of the multiple benign tumor-like new growths of the skin described by Schweninger and Buzzi. The significance of the history of erythematous papules or nodules preceding the lesions, however, is not clear.

DR. H. N. COLE: The two Negro patients present macular atrophy secondary to syphilis. This disorder is rare. The other patient's disorder corresponds to that described by Schweninger and Buzzi. I do not believe that varicella enters into the picture in any of these cases. Varicella produces a scar, while these patients exhibit atrophy.

DARIER'S DISEASE. Presented by DR. JOHN A. GAMMEL.

J. S., a Jugoslavian aged 40, has had an eruption on the back for fourteen years. Two weeks ago tonsillectomy was performed; after this a pruritic erythematous eruption appeared on the central portion of the chest. The patient's general health has been good. The eruption involves the anterior and posterior aspects of the chest, the axillae and the pubic region. The lesions are small light brown follicular papules. Over the chest there is a more acute process superimposed; the latter consists of reddish papules and a few pustules with excoriations. There are no other abnormalities. The Wassermann reaction of the blood was negative.

Biopsy revealed the histologic picture of Darier's disease.

DISCUSSION

DR. H. N. COLE: This is a rather interesting and unusual manifestation of Darier's disease. It is not unusual for patients with such disorders to have a secondary infection, which would explain the acute infectious eczematoid dermatitis present on the chest.

PIGMENTED CICATRIZING NEVUS OF THE NOSE. Presented by DR. E. W. NETHERTON.

M. D., a man aged 49, states that about ten years ago a small dark scaly lesion developed on the right side of the nose, half-way between the inner canthus of the eyes and the ala of the nose. There has never been any ulceration. The spot has gradually enlarged fairly evenly in all directions, and the progressing margin has always been slightly raised and hyperpigmented, while the central portion of the lesion has remained depressed, depigmented and scarred. There has always been a small nodule at the site of the original lesion. At present there is on the right side of the nose and on the adjacent portion of the right cheek an irregular, well defined, noninflammatory lesion, in approximately the center of which there is a nodule the size of a split pea with a small area of melanotic pigmentation on its surface. The greater part of the lesion is smooth and depressed below the normal surface of the skin and consists of a depigmented atrophic-like scar. The margins of the lesion are raised and hyperpigmented. In places this raised margin is threadlike, while along the ala of the nose it is much thicker, somewhat verrucous and more hyperpigmented.

The blood count showed 4,130,000 red cells, 6,800 white cells and 78 per cent hemoglobin. The sugar content of the blood was 118 mg. per hundred cubic centimeters. The Wassermann and Kahn tests of the blood and urinalysis gave negative results. A biopsy showed a moderate keratosis with enlargement of the rete pegs and dermal papillae. There was a relatively large amount of melanin in the pigment in the dermis. There were a few small rather cellular areas in the dermis, associated with melanin pigment suggestive of nevus tissue. The cells did not appear to be actively proliferating. There was no evidence of neoplasm arising from the epidermis.

Grenz ray therapy has been used without any results or apparent change in the lesion. A portion of the margin of the lesion was cauterized with the electric cautery.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: The clinical appearance of the lesion impresses me as being that of basal cell epithelioma, and from examination of the section I thought that this impression was justified.

DR. H. N. COLE: It would be interesting to make another biopsy. From examination of the section I was not willing to make a diagnosis of nevus. There were some characteristics of lupus erythematosus and evidence of scar formation, and I believe that it is not unheard of to find a certain amount of pigment in the papular type of lupus erythematosus. Clinically the lesion suggests epithelioma.

DR. JOHN E. RAUSCHKOLB: I favor a diagnosis of basal cell epithelioma and suggest that attempts be made to determine the characteristics of the pigment by means of the dopa reaction.

DR. E. W. NETHERTON: On first examination the lesion impressed me as being a basal cell epithelioma with pigmentation. However, the possibility of a pigmented melanoma suggested itself. I shall attempt to get a deeper specimen for biopsy.

NOTE.—A second biopsy was made and showed a pigmented basal cell epithelioma. The base was treated with radium.

CONGENITAL SYPHILIS; ENLARGEMENT OF THE STERNAL END OF THE CLAVICLE. Presented by DR. H. G. MISKJIAN.

R. N., a girl aged 16, until three years ago, had frequent convulsions. These were supposed to be due to chronic pyelitis. The patient had pertussis and diphtheria at the age of 7 years, measles and pneumonia at the age of 8 years; a supernumerary digit was excised when she was 3 years old. She has not had scarlet fever or rheumatic fever. She has always been sickly; in infancy she had fre-

quent gastro-intestinal upsets, and in childhood she was frail and nervous. According to the mother there has always been some disproportion in the sternoclavicular region, the left portion being larger than the right.

During the past year, especially during the last three months, the mother has noted a fairly rapid enlargement in the left portion of the sternoclavicular region. At present the patient is fairly well developed, nervous and irritable. The sternal end of the left clavicle is the seat of a fairly extensive diffuse hard but not bony swelling. There is no change in the color of the overlying skin. A scar on the surface represents an incision resulting from excision of a biopsy specimen. The surface of the swelling is raised about 1.5 cm. above the surface. The Wassermann reaction of the blood was 4 plus. Red and white blood cell counts were normal. Urinalysis gave negative results. A roentgenogram made on April 20, 1935, showed that the sternal end of the left clavicle was 2.5 cm. in width while that of the right was 1.5 cm. Cartilage could not be visualized. There was no evidence of destruction or proliferation of bone. There are bilateral cervical ribs, the left being larger than the right. These arise from the eighth cervical vertebra. Biopsy showed masses of hyaline cartilage surrounded by dense fibrous connective tissue. The cartilage cells were sparse in a normal hyaline matrix. There was no hyperplasia and no atypical aggregations of cells. The capsule of the mass was thick and densely fibrous. There was no evidence of tumor formation.

Five hundred roentgens of radiation filtered with 2 mm. of aluminum was administered to the keloidal scar on Aug. 14, 1935. After ten injections of an insoluble preparation of bismuth tartrate and ten injections of mapharsen in doses of 0.03 Gm. each a slight decrease in the size of the mass was noted.

DISCUSSION

DR. H. N. COLE: Periostitis and formation of gumma at the sternal end of the clavicle are fairly common in both congenital and acquired syphilis. The occurrence of supernumerary digits has also been reported in congenital syphilis.

FOX-FORDYCE'S DISEASE. Presented by DR. H. G. MISKJIAN and DR. MAURICE SULLIVAN.

CASE 1.—H. S., a Negress aged 25, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, has an itchy eruption in the axillae and in the perineal and pubic regions. The patient is nervous and introspective and is much distressed over her condition. She says that the itching is almost continuous but that it is much worse during menstruation and when she is under a nervous strain. She complains of backache. There is a chronic vaginal discharge. The eruption consists of discrete follicular papules in the axillae, over the mons veneris and around the nipples; there is no surrounding inflammatory reaction. The eruption is slightly scaly. There is almost complete loss of hair due to scratching.

Roentgenograms of the skull revealed increased sagittal markings. The basal metabolic rate was —12 per cent. Urinalysis gave negative results. The blood cell count showed a normal hemoglobin content and a normal number of red cells; the white cells numbered 5,000. The differential count was normal. The Wassermann reaction of the blood was negative. Examination of the stools gave negative results. The dextrose tolerance test revealed greatly increased tolerance, the sugar content of the blood being 67 mg. per hundred cubic centimeters and a peak of 74 mg. occurring after the dextrose was given.

The results of biopsy were reported as follows: The epidermis showed a fairly marked acanthosis. The interpapillary projections were elongated and thickened. In the middle portion of the section two interpapillary pegs were much larger and deeper than the others. These showed a certain degree of spongiosis. On the outer surface of the epidermis there was a fairly wide area which stained intensely red and showed parakeratosis. Between the upper cells of the malpighian layer and the deeper portions of the parakeratotic area there was some exudation in which fragments of migratory cells were present. On other parts

of the surface one or two small horny plugs were present. The papillary layer of the corium was characterized by a feeble staining quality. The papillae were widened, and many contained dilated blood spaces. Around the aforementioned interpapillary projections there were extensive, though loose, lymphocytic infiltrations along with a number of thick connective tissue cells. A few lymphocytes had forced their way into the epidermis. In the reticular portion of the corium were limited areas of loose perivascular infiltration. A large number of coil glands cut at various angles were seen underlying the corium. These were of the apocrine type; they were perhaps somewhat dilated and at various stages of activity. There was hardly any infiltration around these coils. Much more of infiltration was seen around the hair follicles.

The following therapeutic measures have been used without much apparent result: roentgen irradiations, administration of thyroid, corpus luteum extract and ovarian extract and application of antipruritic ointment.

Case 2.—I. W., a Negress aged 15, presented herself at the outpatient department of the Lakeside Hospital because of a severely pruritic eruption in the axillae of six months' duration. There has been little or no change in the appearance of the eruption during the past three years. Approximately six months ago the pruritus suddenly stopped, and there has been no recurrence of it. In the axillae is a marked papular eruption. The papules are firm and are arranged in parallel lines suggesting planes of cleavage. There is a sparse growth of hair. A few lesions are present also in the pubic region. Urinalysis gave negative results. The blood cell count showed 4,300,000 red cells, 3,800 white cells and 78 per cent hemoglobin. The differential count was normal. The curve for dextrose tolerance was as follows: during fasting, 69 mg. of sugar per hundred cubic centimeters of blood; thirty minutes after administration of dextrose, 67 mg.; one hour after administration of dextrose, 77 mg., and one and one half hours after administration of dextrose, 66 mg. The basal metabolic rate was —20 per cent.

Results of a biopsy were reported as follows: The epidermis showed acanthosis and some degree of spongiosis. The interpapillary projections were surrounded by a lymphocytic infiltrate. The vessels in the corium showed a slight perivascular infiltration. There was an infiltration of exudative cells into the cutis, composed of monocytes, polymorphonuclear eosinophils and neutrophils. There were a number of dilated coil glands of the apocrine type.

In 1933 the patient received 200 roentgens of filtered radiation three times at intervals of two weeks and obtained considerable relief for a few months.

Case 3.—M. C., a girl aged 15, has an eruption which started two years ago with intense pruritus in the axillae and pubic areas. It consists of firm grayish to violaceous follicular papules, some of which show a slight central depression. The lesions are quite numerous and closely packed and show a tendency to arrangement in parallel lines. Urinalysis gave negative results. The blood cell count showed 3,000,000 red cells, 4,200 white cells and 65 per cent hemoglobin. The differential count was normal. The Wassermann reaction of the blood was negative. The basal metabolic rate was —33 per cent. The curve for dextrose tolerance was as follows: during fasting, 77 mg. of sugar per hundred cubic centimeters of blood; thirty minutes after administration of dextrose, 121 mg.; one hour after administration of dextrose, 93 mg., and two hours after administration of dextrose, 144 mg.

Results of biopsy were reported as follows: The epidermis was slightly thicker than normal. There were some new blood vessels in the corium with perivascular infiltration of lymphocytes. Edema and infiltration were observed around several of the sudoriferous glands. There was one lobular collection of hyperplastic and dilated sudoriferous glands (apocrine glands).

The patient has received 0.03 Gm. of thyroid three times a day and pills of ferrous carbonate U. S. P. The basal metabolic rate three months after institution of therapy was —2 per cent. She also received three doses of radiation consisting of 150 roentgens filtered with 1 mm. of aluminum at three week intervals. No improvement has resulted from this therapy.

DISCUSSION

DR. E. W. NETHERTON: It is interesting to note that the basal metabolic rate was reduced in all three cases. I have recently observed a case of Fox-Fordyce's disease in which hyperthyroidism was present. The absence of itching in one patient is also noteworthy. Dr. Miskjian and Dr. Maurice Sullivan are to be congratulated on presenting three patients with this interesting disorder at one meeting.

J. R. DRIVER, M.D., *Reporter*

Regular Meeting, Jan. 23, 1936

H. G. MISKJIAN, M.D., *Presiding*

ACANTHOSIS NIGRICANS. Presented by DR. MAURICE SULLIVAN.

R. G., a Jew aged 20, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, had the usual diseases of childhood but has never had any serious illness. He has had acne for several years. In 1920 he was treated in the outpatient department for a condition described as eczema. In 1926 a diagnosis of seborrheic dermatitis of the psoriasiform type was made. In 1928 he was treated again for seborrheic dermatitis. His present cutaneous trouble started early in 1933, as a more or less generalized eruption, and has gradually become more extensive, affecting especially the lower part of the abdomen, the genitalia, the thighs, the right axilla and the upper portion of the back. The lesions are in various stages of development; some are small and others large. The right axilla is completely filled with one crusted lesion. Some lesions have healed, leaving soft white scars with a brownish pigment at the border. Many of the earlier lesions consist of small hyperpigmented papules. In the flexor areas there is some discharge of seropurulent material. Over the face and upper portion of the back the eruption is of an acneform type. The Wassermann reaction of the blood was negative. Examinations of the blood revealed no abnormalities; cultures for fungi gave negative results. Examination of the stools disclosed no parasites. A roentgen examination of the gastro-intestinal tract showed nothing of importance. Biopsy showed the epithelium to be rather markedly hyperkeratotic, thicker than normal and somewhat irregular. There was pleomorphism of the cells in the epidermis and irregularity of the basal layer. There was no invasion and no disturbance in pigment distribution. In several areas there were dense cells of polymorphonuclear leukocytes associated with focal tissue necrosis and generally with little fixed tissue reaction. There were several sharply circumscribed areas in which the normal corium had been replaced by collections of epithelioid cells, and among these were many small giant cells, which were multinucleated and contained peripherally disposed nuclei. There was no caseation necrosis and no tubercle formation.

DISCUSSION

DR. J. R. DRIVER: Clinically the condition is highly suggestive of acanthosis nigricans. However, the lack of pigment in the biopsy specimen is against this diagnosis, and it may be that the disorder is simply an unusual manifestation of seborrheic eczema with secondary infection resulting in the unusual scarring.

DR. H. N. COLE: The picture is rather unusual. The localization of the lesions is the same as in acanthosis nigricans. I believe that further study will prove this diagnosis to be correct.

BLUE NEVUS. Presented by DR. JOHN E. RAUSCHKOLB.

C. T., a woman aged 22, from the service of Dr. Cole and Dr. Driver at the City Hospital, has had a lesion on the left cheek near the temporal area since

birth. It is speckled and bluish green, and from it grow numerous coarse hairs. By transillumination from the mouth the lesion is plainly visible in the cheek, manifesting itself by numerous dilated and connected vessels which do not pulsate. Deposits of an apparently increased pigment are present in the skin.

DISCUSSION

DR. G. W. BINKLEY: I believe that this lesion is an example of the blue nevus of Jadassohn due to an infiltration of pigment cells rather than to vascular change.

DR. JOHN E. RAUSCHKOLB: I was of the opinion that it was a blue nevus and that is why I presented the patient. I am wondering, however, about the possibility of malignant degeneration, and for that reason I hesitate to remove material for a biopsy.

DR. H. N. COLE: Blue nevi are said not to degenerate.

DR. J. R. DRIVER: The resemblance of this lesion to the type of accidental tattoo seen in coal miners is striking. I agree, however, with the diagnosis of blue nevus.

NECROBIOSIS LIPOIDICA DIABETICORUM. Presented by DR. W. H. CONNOR.

E. G., a Jewess aged 39, from the service of Dr. Cole and Dr. Driver at the City Hospital, has been treated in the outpatient department since 1930 for obesity, thyroid and ovarian hypofunction and diabetes mellitus. In October 1932 she noticed an eruption on the left breast, consisting of two coin-sized plaques; another lesion appeared over the metacarpophalangeal joint of the index finger of the left hand. Some lesions are located on the lateral aspect of the right leg, and there is another lesion just below the right knee on the anterior surface. In 1935 another lesion appeared on the right forearm. The earlier lesions have increased slightly in size. The lesions vary from 4 to 7 cm. in diameter. They are slightly raised and infiltrated and have a violaceous, dull brownish red border. The central portion of the involved area is markedly xanthochromic and shows some telangiectasia.

The Wassermann reaction of the blood was negative. The patient's weight averages 250 pounds (113.4 Kg.). The sugar content of the blood ranges from 147 to 266 mg. per hundred cubic centimeters. The cholesterol content ranges from 142 to 199 mg.

A biopsy was reported on as follows: The epidermis showed occasional mild hyperkeratosis, moderate intercellular edema and some flattening of the rete pegs. The vessels in the papillary layer were slightly dilated, and the collagen was slightly increased. The blood vessels throughout the corium showed thickened walls, narrow lumens and collars of small round cells. There were foci of necrobiotic changes with degenerated homogeneous-appearing fibrous tissue and infiltration with fibroblasts. There were various large and small round cells and spaces which by special stains were shown to be filled with fat. There was also an abnormal content of fat in the degenerative connective tissue. Treatment has consisted of a rigid diabetic diet and administration of insulin. The sugar content of the blood became normal, but there was little or no change in the cutaneous lesions.

DERMATITIS EXFOLIATIVA AND CATARACTS DUE TO DI-NITROPHENOL. Presented by DR. J. M. HITCH and DR. W. F. SCHWARTZ.

The patient is from the service of Dr. Cole and Dr. Driver at the City Hospital. A complete report of this case appeared in *The Journal of the American Medical Association* (**106**:2130 [June 20] 1936).

DISCUSSION

DR. I. L. SCHONBERG: I had an opportunity to see this patient when the disorder first started. The lesions at that time were located generally over the body, but the eruption was not universal. It closely resembled seborrheic eczema. She

was hospitalized at the Mount Sinai Hospital, but in spite of treatment the eruption continued to spread, and she was then transferred to the City Hospital.

DR. H. N. COLE: This case, I believe, is unique in that it is the first that has been reported of an exfoliative dermatitis developing after the ingestion of di-nitrophenol. For this reason I think that the case is worth reporting more completely.

LYMPHOBLASTOMA OF THE MYCOSIS FUNGOIDES D'EMBLÉE TYPE. Presented by DR. W. H. CONNOR.

C. G., a policeman aged 39, from the service of Dr. Cole and Dr. Driver at the City Hospital, states that in December 1934 he began to suffer from a nasal discharge of a seropurulent type. The nose became swollen on the right side. After roentgen treatment totaling 1,500 roentgens given in divided doses there was marked improvement, and the patient returned to his work for five weeks. The process then recurred. The Wassermann reaction of the blood was negative, and a therapeutic test consisting of eight injections of neoarsphenamine resulted in no improvement. On July 1, 1935, the right side of the nose was incised externally and the right antrum was opened. A biopsy made at that time at the Huron Road Hospital was reported to show transitional cell carcinoma. The operative wound refused to heal, and an extensive granulating ulcer resulted. On July 29, 1935, the patient was admitted to the City Hospital. At that time the temperature, pulse rate, respiratory rate and blood pressure were within normal limits. Examination showed that there was no pathologic involvement below the neck. The cervical lymph nodes were slightly enlarged. The nose was approximately twice the normal size, a disproportionate increase being present on the right side. There was a ragged ulcer about 2 cm. in diameter. The nares were practically closed by edema and seropurulent discharge. Both upper middle incisors were absent, and in the socket of the right middle incisor there was a sinus leading to the right antrum. In the midline of the hard palate, 2 cm. posterior to the front teeth, there was a perforating ulcer surrounded by granulations and exuding purulent material.

Urinalysis gave negative results. Complete examination of the blood disclosed no abnormalities other than a progressive secondary anemia. Repeated Wassermann and microscopic precipitation tests for syphilis were negative. A test with tuberculin was positive with a 1:100,000 dilution; a 1:1,000,000 dilution gave a negative reaction. Repeated examinations, cultures and smears for fungi gave negative results. Nonhemolytic streptococci, Staphylococcus albus and Staphylococcus aureus were cultured from the pus. Bacillus mallei was never found. From July until January the following progress was noted: On the left thigh several firm, erythematous nodules in a circinate arrangement developed; ulceration, sloughing and periphereal enlargement followed. On both cheeks firm indurated nodules developed; these started as small lesions and increased to the size of a dollar or larger, showing sharply demarcated borders and superficial ulceration. The lesion on the nose progressed after temporary improvement had resulted from roentgen treatment in fractional doses averaging a total of 3,000 roentgens.

Several specimens for biopsies were taken from new lesions, from the older ulcers and from a lymph node removed from the groin. The following diagnoses were based on these examinations: nevocarcinoma; lympho-epithelioma; transitional cell epithelioma; chronic granulation tissue, and lymphoblastoma. The last diagnosis was based on examination of the lymph node. In November 1935 the left ankle became markedly swollen. Roentgenogram of the ankle showed a line of diminished density at the epiphysis; this was diagnosed as osseous atrophy. In addition to roentgen therapy the patient received injections of foreign protein, intravenous injections of metaphen, local applications, etc.

DISCUSSION

DR. R. E. BARNEY: The disorder is unusual, and I believe that it is mycosis fungoides d'emblée. I recall that in Dr. Keim's monograph on lymphoblastoma there is a report of one case of mycosis fungoides in which the first lesion appeared in the mouth; later lesions developed on the body.

DR. J. R. DRIVER: When the patient first presented himself at the hospital the lesions were limited to the palate and nose. At that time the question of mixed tumor presented itself. I was of the opinion that this lesion, which presented a microscopic picture of lympho-epithelioma and transitional cell carcinoma, had originated as a mixed tumor. However, subsequent biopsies from a metastatic lesion in a lymph node in the groin make the diagnosis of lymphoblastoma more likely.

DR. JOHN E. RAUSCHKOLB: It has been interesting to follow the course of the disorder while the patient was in the hospital. When the nodular lesions of an erythematous type appeared on the thigh they resembled erythema multiforme or erythema nodosum. Examination of material from one of these lesions at that time revealed only chronic inflammatory tissue. I was of the opinion that this manifestation was a toxic erythema resulting from absorption of degenerative neoplastic tissue on the face following irradiation.

DR. H. N. COLE: My associates and I have been following this case for several months. There have been many conflicting and confusing factors. At times the clinical appearance of the lesion was that of a syphiloderm. However, at present from the clinical and from the pathologic evidence I believe that the disorder is a lymphoblastoma of the mycosis fungoides d'emblée type.

NOTE.—During almost his entire stay in the hospital the patient became progressively worse. He died on Feb. 9, 1936, of bronchopneumonia. A brief résumé of the autopsy observations is as follows: The disease was generalized, lesions being present on the skin, in the lungs, in the left testicle and in the lymph nodes. The primary lesion originated in the mucosa of the nose. The diagnosis of lymphoepithelioma based on microscopic interpretation of two intermingling cell types resulted from the mistake of considering what were really degenerated epithelial cells as lymphoid cells. Microscopic studies from the metastatic lesion showed the process to be lymphosarcoma.

NEUROTROPHIC LESIONS ON THE RIGHT SIDE OF THE FACE FOLLOWING THROMBOSIS OF THE LEFT POSTERIOR INFERIOR CEREBELLAR ARTERY. Presented by DR. W. H. CONNOR.

G. W., a man aged 50, from the service of Dr. Cole and Dr. Driver at the City Hospital, has been suffering from diabetes mellitus and a hypertensive vascular disease. In November 1934 while he was in bed, the patient awoke perspiring profusely; he complained of numbness of the left side of the face and was unable to stand. A few days later vesicles appeared on the lips and on the left cheek; these began to crust and scale; then they healed, leaving atrophic scars. At this time some of the lesions on the cheek have not entirely healed; they have been extremely chronic. Clinically they resemble lupus erythematosus.

Neurologic examination revealed a slow, coarse, clockwise rotary nystagmus when the patient looked to the left and a fine, rapid lateral nystagmus when he looked to the right. There was sensory impairment to light touch and pinprick in the entire left side of the face excepting a small area at the angle of the mandible. There were slight weakness of the left lower portion of the face and a moderate degree of deficiency of hearing in the left ear. There was marked ataxia of the legs, but no definite localization of this ataxia to either side could be demonstrated. There was impairment in sensation to pinprick in the left leg. In the opinion of Dr. R. E. Stout of the neurologic department, these findings represent a thrombosis of the posterior inferior cerebellar artery or cerebellar apoplexy.

DISCUSSION

DR. W. H. CONNOR: This patient has been under observation for quite a long time now, and my co-workers and I are indebted to the neurologic department for finally clearing up the diagnosis. At different times the lesions have been considered to be blastomycosis, lupus erythematosus, bromoderma or iododerma. All attempts to prove any of these diagnoses were unsuccessful. A biopsy from one of the lesions simply showed a certain amount of hyperkeratosis, acanthosis and mild chronic inflammation.

SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

JOHN M. GRAVES, M.D., *Secretary*

Jan. 24, 1936

C. J. LUNSFORD, M.D., *President*

BULLAE IN SCLERODERMA. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

Mrs. W. was presented before this society in April 1935 (ARCH. DERMAT. & SYPH. **33**:571 [March] 1936) because of an eruption which consisted of bullae superimposed on patches of scleroderma. A factitious dermatitis was also considered at that time. The condition has persisted to date. The section which is shown is suggestive but not typical of scleroderma. The patient states that she has not taken or applied any drugs.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: For approximately two years this patient has suffered from lesions which developed slowly, beginning as indurated areas from the size of a dime to that of a quarter. The lesions which I have observed are ivory colored and violaceous at the border. That is the first stage. In the second stage extensive bullae such as the patient exhibits at present form over the lesions. Hemorrhage occurs into the bullae. The next stage can be seen in the lesion over the sternum and consists of a drying and crusting of the bullous lesion. The last stage, exhibited in the lesion in the left scapular region, consists of atrophy.

The patient states that the bullous stage at times lasts for two to three months.

I believe that the pathologic picture is compatible with scleroderma, as evidenced by swelling of the individual collagen fibers and thickening of the whole collagen layer. There are two types of bullous formation: one subcorneal and one in the papillary layer.

DR. A. E. INGELS: It seems to me that there is nothing in the picture that suggests scleroderma. The skin is soft and pliable. The whole lesion can be lifted up without great difficulty. Moreover, I should say that the pathologic picture is against scleroderma. There is formation of myxoma-like cells beneath the basal layer. This does not fit in with scleroderma. Without sections stained for mucin and amyloid a diagnosis cannot be made. I would hesitate to classify the lesions before seeing the results of differential staining; I should wish to see not only sections stained with hematoxylin and eosin but also sections stained for mucin and amyloid as well as for connective and elastic tissue.

DR. H. J. TEMPLETON, Oakland, Calif.: I have observed two cases of amyloid degeneration of the skin. In neither of them was the appearance like that exhibited by this patient; it more closely suggested patches of lichen simplex chronicus.

DR. G. V. KULCHAR: The section I saw tonight was compatible with a diagnosis of an early stage of scleroderma. Edema is frequently a feature of the early stage of scleroderma, and there is only a short step from edema to bullous formation. The occurrence of bullae in cases of scleroderma is rare but has been reported.

DR. A. E. INGELS: How could the presence of myxomatous cells in scleroderma be explained? That association has never been reported.

DR. N. N. EPSTEIN: I think that clinically the lesions before the appearance of the bullae could well be scleroderma. I disagree with Dr. Ingels that the upper layer is myxomatous. This tissue suggests the formation of young connective tissue. I should like to see other slides and stains for confirmation.

MYCOSIS FUNGOIDES. Presented by DR. N. N. EPSTEIN and DR. H. J. TEMPLETON, Oakland, Calif.

Gus S., aged 48, is presented to show the effect of fever therapy in mycosis fungoides. He has been presented before this society previously. The histologic picture is typical of mycosis fungoides.

The eruption began in 1929 and has gradually progressed until it is now in the ulcerating tumor stage.

Therapy has consisted of roentgen radiation as needed. Arsenic was administered in 1931 in the form of solution of potassium arsenite. Two intravenous injections of typhoid-paratyphoid vaccine were given in 1931, with no benefit. Intramuscular injections of ethyl chaulmoograte administered for two months in 1935 produced no improvement. In December 1935 the patient was referred to Dr. N. N. Epstein for fever therapy. To date he has received six treatments of five hours each, during which time his temperature was elevated to 40 C. (104 F.) for thirty hours. Fever was induced by the blanket pack method.

DISCUSSION

DR. N. N. EPSTEIN: Recent reports on the use of fever in mycosis fungoides indicate that fever does have some effect on the course of that disease. The results are certainly not startling, but something does happen to the process that seems to reduce the activity. The lesions become less red, and tumors have even been known to disappear. My co-workers and I have tried to use fever therapy before in cases of mycosis fungoides by attempting to inoculate the patients with erysipelas, but we were unsuccessful. We also attempted to produce fever by diathermy, but severe burns resulted. Now we have a method of wrapping the patient in blankets and furnishing heat from an external source, which raises the temperature to the desired height. This man has tolerated the treatment very well. When the patient comes for treatment now he walks into the hospital, and he is quite well as far as strength and weight are concerned, but I do not think that anything except some relief can be expected from the treatment.

I do not think that his tumors have changed. There are areas on his legs that become paler after treatment. He is more comfortable. His feet are softer.

The use of malaria suggests itself. I believe, however, that malaria is too debilitating to use on a patient in this state.

DR. H. J. TEMPLETON, Oakland, Calif.: This case proves that itching is not necessarily a feature of mycosis fungoides.

DR. N. N. EPSTEIN: Dr. W. J. Kerr has tried several times to inoculate erysipelas, but he has been unable to transmit the disease.

DR. MERLIN MAYNARD, San José, Calif.: What method of inoculation was used?

DR. N. N. EPSTEIN: Serum from bullae was injected intradermally.

DETROIT DERMATOLOGICAL SOCIETY

G. WARREN HYDE, M.D., *Recorder*

Jan. 21, 1936

LOREN W. SHAFFER, M.D., *President*

A CASE FOR DIAGNOSIS (RHINOPHYMA-LIKE ENLARGEMENT OF THE NOSE; SARCOID?). Presented by DR. THOMAS H. MILLER.

R. C., a Negro aged 30, married, born in Georgia, complains of enlargement of the tip of the nose. The patient's father, mother, wife and children are living and well.

The patient was first seen in 1933; at that time he had a generalized lymphadenitis. A diagnosis of tuberculosis was made, being based on the results of biopsy. There was no evidence of pulmonary tuberculosis. He also presented a bluish red lesion on the nares which had appeared after squeezing of a pimple. A diagnosis of rosacea was made; that of an angiolupoid was also considered.

The patient was not seen again until today. There is a large bluish red infiltrated soft and bulbous lesion at the tip of the nose with rather indistinct borders which fade into the normal skin. No atrophy, ulceration or apple jelly nodules are present. Enlarged venules course over the surface of the involved area. No tenderness or inconvenience is associated with the disorder.

The patient states that after he was last seen, while he was working outside on a cold day the nose suddenly became enlarged and that it has remained about the same up to the present time.

DISCUSSION

DR. JOHN RAUSCHKOLB, Cleveland: I think that the disorder is sarcoid. I believe that a biopsy, roentgen examination of the chest and tests with graded dilutions of tuberculin would help in establishing the diagnosis.

DR. HARTHER L. KEIM: It seems to me that this lesion is not simply a dilatation or a hypertrophy of the glands but rather a granulomatous mass, and I believe that a biopsy might show some evidence of tuberculosis. I think that all the members have seen such lesions in Negroes. I do not recall having seen any as extensive as the tumor of the nose exhibited by this patient, but the lesions are often associated with changes in the bones of the fingers, and I suggest that roentgenograms of the hands be made.

PROF. FRANZ BLUMENTHAL, Ann Arbor, Mich.: I agree with Dr. Rauschkolb's diagnosis.

LICHEN PLANUS SCLEROSUS ET ATROPHICUS (HALLOPEAU). Presented by DR. CYRIL K. VALADE.

A. B. J., a man aged 32, married, born in the United States, states that in 1932 an eruption appeared on the left flank, spreading to the right flank, then to the back and later to the extremities. The patient has experienced no sensations referable to the cutaneous disorder.

There are atrophy and flat-topped white papules. The lesions are both discrete and grouped to form plaques. In the large areas small papules may be seen along the edges. The lesions grouped on the left wrist are glistening pearl-like striated papules. Some are elevated, and all are firm to the touch. The large atrophic areas are fawn colored. There is plugging of the follicles and of the pores.

The sections show at one end a bandlike infiltrate of mononuclear cells such as is commonly seen in lichen planus, but the other changes associated with lichen planus, particularly increase in the granular layer, are not evident. The remainder of the section shows a markedly atrophic epidermis, and under this the papillary body is distinctly sclerotic.

DISCUSSION

DR. B. F. BARNEY, Ann Arbor, Mich.: I was not sure of the diagnosis. The disorder is probably some variety of morphea. At first I did not notice the needle-like plugging, but on repeated examination I did find such plugging on the wrists, and I think that the diagnosis made by the presenter is justified.

DR. GEORGE H. BELOTE: I examined the microscopic sections before I saw the patient. I thought that the slide had some of the characteristics of ordinary lichen planus. However, there were also areas of distinct sclerosis in the section, particularly in the upper third of the corium, and as far as I know it is not common for lichen planus sclerosus et atrophicus of the Hallopeau type to produce the sort of infiltrate exhibited by this patient. Ordinarily if any infiltrate is present in that condition it is deeper than in this section, and consequently in my report to Dr. Valade I said that there was some question in my mind as to whether the disorder was true lichen planus of the Hallopeau type or lichen planus with atrophy.

After looking at the eruption I am still undecided. On account of the infiltrate, however, I favor the diagnosis of lichen planus with atrophy more than that of the true lichen planus atrophicus et sclerosus of Hallopeau.

DR. HARTHER L. KEIM: I think the disorder is a borderline condition. In the current year-book this sort of condition is grouped under white spot disease.

TUBERCULID. Presented by DR. ROBERT C. JAMIESON.

M. A. K., a woman aged 22, single, unemployed, was presented in December 1934.

DISCUSSION

DR. GEORGE H. BELOTE: The nodules on the face are rather deep-seated; they are purplish and have a doughy feel. The appearance suggests paraffinoma. Dr. Shaffer suggested the diagnosis of sarcoid when the patient was presented in 1934. A few months later she appeared at the clinic at Ann Arbor, Mich., and a biopsy was made. The section suggested tuberculosis. The patient has since been treated by Dr. Jamieson, with the result that the infiltration has practically disappeared but there is marked scarring.

DR. ROBERT C. JAMIESON: I presented the patient in order to show the results of roentgen treatment of paraffinoma. I saw her after the diagnosis of tuberculosis had been made at Ann Arbor, Mich., and more as an experiment than because I expected definite results I gave her some small doses of filtered roentgen rays. After two or three treatments the normal contour of the cheeks appeared; the swelling disappeared, and the improvement progressed until the present stage was reached. There is a slight atrophy of the subcutaneous areas in certain places.

DR. LOREN W. SHAFFER: What amount of roentgen rays was used and what was the individual dose?

DR. ROBERT C. JAMIESON: The doses were small and were administered at weekly intervals. I cannot recall offhand exactly how much radiation was given.

DR. A. R. WOODBURNE, Grand Rapids, Mich.: There are two little scaly areas on the nose that look like lupus erythematosus. I do not believe that those lesions were present when the patient was seen before.

DR. ROBERT C. JAMIESON: I think that they were present at the time and are practically unchanged.

REPORT ON A CASE PREVIOUSLY PRESENTED. DR. ARTHUR E. SCHILLER.

A patient was presented last month with the diagnosis of hatband dermatitis. The suggestion was made that the disorder might be lupus erythematosus or an eruption due to phenolphthalein. The patient was given phenolphthalein, and there was no flare-up of the eruption, two patch tests with a piece of the hatband made at different times produced a marked reaction on the arm. It was hoped that the patient would come today because both reactions are still visible.

LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W. NISBETH, M.D., *Secretary*

Jan. 14, 1936

NELSON PAUL ANDERSON, M.D., *Chairman*

A CASE FOR DIAGNOSIS. Presented by DR. H. P. JACOBSON.

R. K., a woman aged 44, a Hungarian housewife, states that when she was 2½ years old she was burned extensively by hot water. The burns healed, leaving a small red area on the right ear and at the left angle of the mouth. At that time an area of erythema appeared on the posterior aspect of the left thigh. The lesion on the face disappeared, but that on the leg has been growing slowly. About four years ago the lesion on the ear began to enlarge after the patient had a serious cold.

On the lower half of the right ear there is a lesion which extends forward about 1 inch (2.5 cm.). There are also a palm-sized area of erythema on the posterior aspect of the left thigh and a white scar 3 cm. in length at the left angle of the mouth. A Wassermann test made on Feb. 5, 1935, gave a 4 plus reaction. There is no history of a primary lesion.

Treatment since February 5 has consisted of ten injections of 0.13 Gm. of bismuth subsalicylate, ten injections of 3 Gm. of neoarsphenamine and three injection of 0.13 Gm. of bismuth subsalicylate. The patient has also received applications of ammoniated mercury ointment and cod liver oil and malt extract internally.

No acid-fast organisms were found in a smear made on Feb. 13, 1935; a culture also gave negative results. A biopsy made on Feb. 9, 1935, showed lupus vulgaris. According to another report (Feb. 25, 1935) the changes were more like those of tuberculosis of the skin than like those of syphilis.

DISCUSSION

DR. SAMUEL AYRES JR.: I think that this disorder is an interesting example of the tumid variety of lupus erythematosus, although it possesses features of lupus vulgaris. Possibly it belongs in the category of disorders exhibiting characteristics which make it difficult to differentiate between lupus erythematosus and lupus vulgaris.

DR. SAUL S. ROBINSON: I agree with the diagnosis of lupus vulgaris.

DR. L. F. X. WILHELM: The fact that the lesion has been present for forty-four years rules out syphilis. I agree with the diagnosis of tuberculosis.

DR. H. S. CAMPBELL: I agree with the diagnosis of lupus vulgaris.

DR. H. P. JACOBSON: I know little about this case. I saw the patient for the first time about three months ago at a meeting at which she was presented with the diagnosis of malignant degeneration of the skin. After that I did not see her for three months; then she again came to the clinic, presenting an eruption involving the right ear and the left thigh, the characteristics of which were essentially similar to those now present. Without having had an opportunity to study the slides microscopically I present the patient with a clinical diagnosis of lupus vulgaris of the left thigh and sarcoid of the right ear.

ROSACEA-LIKE TUBERCULID OF LEWANDOWSKY. Presented by DR. SAUL S. ROBINSON.

R. M., a woman aged 25, whose family history discloses no evidence of tuberculosis has an eruption on the face which appeared suddenly six months ago. On the cheeks and chin are areas of closely set papules from the size of a pinhead to that of a millet seed on an erythematous base. A few pustules and scaling papules are interspersed. Examination with the diascope reveals apple jelly pigmentation in many papules. The patient states that a biopsy made by Dr. S. W. Becker, of the University of Chicago, several months ago showed rosacea-like tuberculid of Lewandowsky. The patient states that she received ten injections (gold preparation?) in Chicago and that some clearing of the eruption followed that treatment.

DISCUSSION

DR. L. F. X. WILHELM: I think this is an interesting disorder. So far as I recall, it is the first time I have seen this particular type of tuberculosis. According to the history the microscopic picture has definitely shown tuberculosis of the skin.

DR. H. S. CAMPBELL: I think the clinical picture is absolutely typical of what it represents. The disorder is rather rare. In approximately two years at the Hôpital Saint Louis, in a well attended outdoor clinic held daily in a community where tuberculids were of comparatively common occurrence, only six cases of this disorder were observed.

DR. MOSES SCHOLTZ: I should call this disorder an acne-like but not a rosacea-like tuberculid. There is no telangiectasia. The skin is dry. If any-

thing can be compared with this condition it is a necrotic acne. I think that the term rosacea-like is used entirely too loosely.

DR. KENDAL FROST: It seems to me rather important to keep to the terminology when a name such as rosacea-like tuberculid of Lewandowsky is given to the condition. It has certain morphologic and prognostic significance.

DR. SAUL S. ROBINSON: So far as I know this is the first case of rosacea-like tuberculid of Lewandowsky presented before this society. The first cases in this country were recorded by McKee, Sulzberger and Wile. This condition has been recognized in Europe since 1917, but only during the past few years have a few cases been observed in this country. In lupus miliaris faciei the lesions are deeper, no pustules occur and no erythema or violaceous hue, as exhibited by this patient, is present. The histologic picture of rosacea-like tuberculid shows no caseation as does that of lupus miliaris faciei.

ARSENICAL DERMATITIS LASTING SIX MONTHS. Presented by DR. IRVING R. BANCROFT.

I. M., a man aged 22, a Mexican, says that his father had syphilis. He exhibits phthisis bulbi, left nystagmus and some atrophy of the optic nerve. From July 1934 to July 1935 he received thirty-four injections of an arsenical preparation. The administration of arsenic was discontinued in August 1935, when the rash first appeared. Sixty-four injections of a bismuth preparation have been given since then, the treatment being continued up to last week. The general appearance is good. There are numerous oval dry and scaly erythematous itching patches on the body, and on the anterior aspect of both forearms there is a diffuse, sharply marginated moist bright red itching rash. This rash has not changed much in the last few months. Seven Wassermann tests have been made; the reactions have been mostly 1 or 2 plus. Scrapings from lesions were negative for mycelia. Culture also gave negative results.

DISCUSSION

DR. H. P. JACOBSON: This is a type of disorder which, I am sure, no dermatologist is eager to treat, as its response to therapy is at best rather slow. I am now treating a female patient who presents an eruption closely similar in character to that exhibited by Dr. Bancroft's patient. Her lesions consist of oval or circular plaques, sharply marginated and elevated, resembling for the most part a seborrheic dermatitis but now and then closely simulating pityriasis rosea. Some of the lesions may also be mistaken for tinea. I am of the opinion that the eruption is a result of bismuth rather than of arsenic medication. It is probably a manifestation of allergy engendered by an altered cutaneous reaction to a combined bismoprotein factor. The prognosis, as already indicated, is a slow response to therapy, but, on the whole, it is much more hopeful than in the diffuse erythematosquamous type of reaction engendered by arsenic.

DR. H. C. L. LINDSAY: I was impressed by the great resemblance between this type of dermatitis and mycosis fungoides.

DR. SAMUEL AYRES JR.: I am rather inclined to believe that the picture is due to the bismuth medication, although that cannot be proved. My co-workers and I recently had a patient in whom an eruption appeared on the hands and feet and on some parts of the body during treatment with bismuth only; we regarded the disorder as being due to bismuth. I think that this is one argument against concomitant administration of bismuth and arsenic. I think that any eruption appearing in the course of anti-syphilitic treatment calls for the discontinuance of all treatment, at least temporarily. The configuration of these lesions is interesting. They are oval and follow the lines of cleavage of the skin like pityriasis rosea.

DR. MOSES SCHOLTZ: I think that the diagnosis of eruption due to a drug is accepted too easily. The fact that a patient has been taking bismuth is no proof that an eruption exhibited by that patient is due to the drug. In this case the patches are entirely too well defined to be of medicinal origin, and the mere

fact that the rash spreads when administration of arsenic is continued does not prove that it is due to arsenic. It might be an acute psoriasis which is aggravated by arsenic. Only few eruptions due to bismuth are seen in this country. A rash due to a drug should be more diffuse than that exhibited by this patient, and it would be associated with some other signs of intolerance to the drug. I should not accept this diagnosis until it is proved more conclusively. The disorder may just as well be a mycotic infection.

DR. C. R. HALLORAN: The picture is that which is frequently seen in eczema. Irrespective of whether the drug administered was bismuth or arsphenamine, the causative agent in these disorders is arsenic.

DR. STANLEY CHAMBERS: I agree with Dr. Jacobson regarding the fact that the disorder is due to bismuth. The follicular character of the lesions and the pityriasis rosea-like configuration are consistent with this diagnosis. The patient has received an equal number of injections of a bismuth preparation and of arsphenamine.

DR. IRVING R. BANCROFT: I thought that the dermatitis was due to arsenic, and I discontinued administration of the drug. Administration of bismuth was continued until recently. It is my opinion that the disorder was originally due to arsenic medication, that the bismuth therapy kept it active and that the latter should be discontinued while the eruption is as severe as it is at present.

CARCINOMA OF THE BREAST. Presented by DR. MOSES SCHOLTZ.

R. R., a woman aged 71, has had high blood pressure. Five years ago she underwent an operation for the removal of the gallbladder and of gallstones. The menopause occurred about twenty years ago. A sore and breaking out at the nipple of the left breast appeared three years ago. This cleared up under treatment at the White Memorial Hospital, where the patient was treated with radiation. Finally she was advised to have the breast amputated—which she refused. Roentgenograms of the chest on Oct 11, 1935, showed solid diffuse shadows, suggesting metastases to both lungs. The patient is a heavy women. The entire left breast is infiltrated; it measures 6 by 7 cm. and is ulcerated in spots. The axillary gland is not palpable. After the cauterized surface healed, peculiar superficial, dark red, slightly scaly, in places moist, irregularly shaped patches appeared on the involved breast. The heart is enlarged toward the right. The blood pressure is 190 systolic and 90 diastolic. Urinalysis showed no albumin; the reaction for sugar was 4 plus. The sugar content of the blood was 138 mg. per hundred cubic centimeters. Treatment has consisted of the Percy cautery and intensive roentgen radiation to the right axilla.

DISCUSSION

DR. SAMUEL AYRES JR.: I believe that the disorder is a carcinomatous manifestation. Whether it is a true Paget's disease I do not know.

DR. H. P. JACOBSON: I see nothing mysterious about the cutaneous lesion that this patient presents. She is suffering from Paget's disease of the left breast, which, as is well known, is an intra-epithelial or intra-epidermal malignant process. The lesion may have its origin in the epidermal layers of the cutaneous covering or in the milk ducts. In either event the process eventually becomes deep seated, involving the glandular substance of the breast as well as the cutaneous covering of that organ. One of the characteristic cutaneous manifestations in this type of cancer is the eczematoid stage of the skin of the breast, and that is exactly what this patient presents—a sharply marginated infiltrated eczematoid eruption of the skin of the involved breast.

DR. KENDAL FROST: I have seen one or two instances in which the cancer involved the skin, exhibiting flame-shaped infiltrations radiating from the primary source or the operative scar, a condition which I regard as a form of cancer en cuirasse.

DR. H. P. JACOBSON: In reply to Dr. Frost's remarks I wish to say that cancer en cuirasse is a definite clinical entity. It consists of an extension of a

malignant focus to the surrounding cutaneous covering. The eruption consists of numerous indurated, solid nodules of various sizes and shapes, discrete for the most part but sometimes confluent, and of an associated infiltration and discoloration of the intervening skin, the color varying from bright to dark red. This patient presents no such manifestations, but she does have a characteristic sharply marginated and somewhat crusted eczematoid eruption, which is a manifestation of Paget's disease.

DR. L. F. X. WILHELM: I regard the disorder as an early stage of Paget's disease of the breast associated with malignant degeneration. Sections from these patches should be taken for microscopic study.

DR. MOSES SCHOLTZ: The diagnosis of Paget's disease is correct except for the fact that it is made four months too late. The nipple was destroyed a long time ago. These cutaneous lesions have developed within the last month or two. There is no trace of the nipple left. I am at a loss to account for the lesions. They are superficial and are not associated with induration. They are developing rapidly and are scattered around. A month ago there was only one patch, and now there are four or five. There is a diffuse infiltration of the skin of the chest. As the patient refused radical operation I used the Percy cautery.

EPITHELIOMA. Presented by DR. IRVING R. BANCROFT.

D., a man aged 59, a cigar dealer, states that he had a chancroid twenty-five years ago. Four or five years ago he noticed a red spot on the face. No treatment was given until June 1935, when, after a Wassermann test gave positive results, antisyphilitic treatment was instituted. The lesion was cauterized two months ago. No improvement occurred. Six roentgen treatments consisting of exposures of fifteen minutes each were given. The last treatment was given two weeks ago. The lesion consists of an ulcer and a crusting fungous growth the size of a 50 cent piece. There is no pain or discomfort. The gland in the neck is enlarged. The microscopic diagnosis was epithelioma of the third grade.

DISCUSSION

DR. H. P. JACOBSON: This case is instructive and illustrates the necessity of revising some of the technic in the handling of malignant cutaneous degeneration. I also wish to emphasize the necessity of adequacy when treating cancer in any form. Regardless of what method of treatment one may employ in the handling of malignant lesions, the principal consideration must be adequacy of technic. This patient was treated with electrosurgery, roentgen and radium radiation, etc., but none of these methods seems to have been employed with sufficient adequacy to have brought about destruction of the malignant process. He now presents an extensive carcinomatous involvement which if neglected much longer will result disastrously. I also wish to call attention to the fact that infiltration anesthesia was employed by the attending physician in the electrosurgical procedure. I condemn the use of infiltration anesthesia in the management of malignant cutaneous degeneration. In my opinion, the method of choice in handling such disorders is actual cautery, especially in the present case; if an anesthetic should become necessary, general anesthesia in one form or another should be employed.

DR. SAMUEL AYRES JR.: Why does Dr. Jacobson object to infiltration anesthesia? If the infiltration is made widely and deeply without striking any cancerous tissue, I fail to see how any damage can occur. The removal by cautery is certainly a fine method of treatment, but it is not the only treatment, and it may not even be the treatment of choice. I should use the endotherm knife and heavily cauterize the base and sides. I fail to see why that method is not applicable.

DR. CHARLES R. CASKEY: I cannot agree with Dr. Jacobson's ideas about anesthesia. In private practice one has to treat many patients with several

epitheliomas. I am afraid the majority of them could not be treated without an anesthetic. I do not think that the infiltration spreads the cancer.

DR. IRVING R. BANCROFT: The only question in this case concerns the form of treatment. The patient has had syphilis, and syphilitic treatment, cautery and roentgen irradiation—the last treatment being given about two weeks ago—have been used. The biopsy shows third grade epithelioma. I think that any kind of irradiation is definitely contraindicated because of previous treatment of that type. I think that the only thing to do is to use a cautery and that the procedure should be carried out by some one who is not afraid to spoil the patient's face.

HERPES ZOSTER. Presented by DR. SAMUEL AYRES JR.

This Negress states that her present illness is of three weeks' duration. It developed while she was receiving neoarsphenamine for syphilis. Slight itching and burning are present. The eruption involves the flexor aspect of the fourth finger of the right hand and extends across the palm onto the wrist and up the medial aspect of the forearm half-way up to the elbow. The lesions occur as discrete and grouped vesicles; the group is not larger than a navy bean, and the vesicles are small.

DISCUSSION

DR. IRVING R. BANCROFT: The patient states that the only way she can stop the itching and burning is to prick the vesicles and let the fluid out. I think that the disorder is herpes zoster.

DR. H. C. L. LINDSAY: The disorder resembles lichen planus. This patient has received a certain amount of arsenic, and arsenic produces lesions that resemble lichen planus.

DR. C. R. HALLORAN: The lesions are lichenoid and deeply pigmented. The diagnosis of lichenoid type of eruption should be considered. I cannot discern the features of herpes zoster.

DR. L. F. X. WILHELM: Last Monday I saw the patient in a good light. There were definite groups of vesicles. While I considered the diagnosis of linear lichen planus, I favored that of herpes zoster.

DR. SAMUEL AYRES JR.: The points brought out here are exactly the ones my co-workers and I considered when we first saw the patient. I am still not convinced that the diagnosis of herpes zoster is correct. The patches themselves are small, and the eruption has the appearance of an annular lichen planus. The disorder is interesting.

DR. STANLEY CHAMBERS: My co-workers and I have observed the same picture in a male patient, and we considered the diagnosis of herpes zoster and that of lichen planus. The histologic picture was that of a lichen planus.

DR. KENDAL FROST: I was impressed by the resemblance of those lesions to lichen planus annularis linearis.

LOCALIZED MYXEDEMA OF THE LEGS. Presented by DR. SAMUEL AYRES JR.

H. I., a man aged 47, underwent partial thyroidectomy for exophthalmic goiter four years ago. Lesions appeared on the legs about one year after the thyroidectomy was performed and have not disappeared. Exophthalmos is present. The eruption is limited to all aspects of the lower portion of the legs, the greatest involvement anteriorly extending two thirds of the way to the knee on the left and half-way to the knee on the right. The eruption consists of numerous discrete and almost confluent slightly pinkish, marble-like doughy nodules with a slightly verrucous feel which consist of tiny flat warty structures. There is no pitting edema. When the skin is stretched the orifices are seen to be considerably dilated. The tonsils are large and cryptic. Transillumination of the frontal sinuses showed dulness. The antrums, especially the right, were dark. Transillumination of the gums gave negative results. Before operation, four years ago, the basal metabolic rate was + 51 per cent. On Sept. 4, 1933 it was + 34 per cent. No treatment has yet been given for the cutaneous condition.

DISCUSSION

DR. W. H. GOECKERMAN: I have seen about half a dozen proved cases of localized myxedema, but I must say that so far as the clinical picture is concerned, that presented by this patient is definitely different from any I have seen. The number of the lesions, the distribution and the purplish hue are different. The ordinary type of localized myxedema is described as being pigskin-like in appearance, and that, I think, is a good description. This patient's lesions do not have that appearance. Yet after a careful consideration of the differential diagnosis, the only diagnosis I can make, chiefly on the basis of exclusion, is localized myxedema. However, the disorder presents a clinical picture definitely different from the manifestations I have seen previously. A careful histologic study should clench the diagnosis if it is correct.

DR. MOSES SCHOLTZ: The disorder impressed me as being rather a paradoxical phenomenon. Maybe it is myxedema. On the other hand, I should like to have an explanation, considering the fact that the patient exhibits signs of hyperthyroidism, extreme exophthalmos and sweating.

DR. KENDAL FROST: Dr. Scholtz' remarks are interesting in view of the fact that at the last examination the patient's metabolic rate was + 34 per cent

DR. STANLEY CHAMBERS: I agree with the diagnosis.

DR. SAMUEL AYRES JR.: This is the first case of this condition I have ever seen. The combination of exophthalmos and a high basal metabolic rate together with localized myxedematous changes seems contradictory. The cutaneous lesions appeared six months after the patient underwent an operation for exophthalmic goiter. Two types of lesions have been described—nodular and plaque-like. I think that this is an intermediate disorder; some of the lesions are nodular; some appear in plaques. The question of therapy is a serious one. Some disorders of this type resist all forms of therapy. A few good results have been reported from the use of iodine and thyroid together. Apparently the normal secretion of thyroid is almost lacking in patients with this disorder. At the same time there is a toxic secretion of the thyroid which produces exophthalmos and a high basal metabolic rate. It is rather confusing to see all these manifestations in the same patient.

DR. W. H. GOECKERMAN: All observers agree that histologically, tinctorially and histochemically the changes in the tissues are not the same as those of a true myxedema. The name is simply a term applied to lesions of this type in this country which has become popular. There are other terms more descriptive. "Myxedema" is really a misnomer. Dr. Ayres' brief dissertation describes the usual course of events in cases of this disorder.

MANHATTAN DERMATOLOGIC SOCIETY

MIHRAN B. PAROUNAGIAN, M.D., *Secretary*

Jan. 14, 1936

PAUL E. BECHET, M.D., *Chairman*

A CASE FOR DIAGNOSIS (ERYTHROPLASIA?). Presented by DR. GEORGE C. ANDREWS.

E. F., a man aged 37, states that about seven months ago he noticed slight itching in the coronal sulcus. For two or three months the irritation would flare up and then regress. Last fall the patient observed two macular areas, one on each side of the frenum. These enlarged peripherally. Urologists considered

the disorder to be a chronic balanitis resulting from incomplete circumcision. Circumcision was performed again one and one-half months ago; after that the lesions joined in the midline to form one sharply outlined red macular area. There was no induration. Apparently the lesion healed at times as a result of application of bland ointments and then recurred. There was no scaling until one month ago. The Wassermann and the Kahn test were negative. The patient has taken about one tablet of allylisopropyl barbituric acid and aminopyrine every three weeks during the past few months.

Microscopic examination showed thickening of the epidermis due to acanthosis. There was no dyskeratosis. The interpapillary areas contained some hydropic cells. In the cutis there was a congestion of the blood vessels, and moderate perivascular cellular infiltration was observed.

DISCUSSION

DR. GEORGE M. MACKEE: It is always difficult to make an unequivocal diagnosis in cases of this disorder because at present a complete composite clinical and histologic concept of erythroplasia is lacking. In most cases there is free exudation; in this case no exudation has been present, but perhaps there is a dry type of erythroplasia. Erythroplasia is supposed to be always sharply marginated. This patient's lesion is well marginated except at one point. There are a number of papular satellite lesions, which are not supposed to occur in erythroplasia but which, however, may prove to be a part of the picture after more is known about the disease. Erythroplasia, like Paget's disease, is not supposed to improve spontaneously; that is, it shows no remissions and exacerbations. According to the patient's statement this lesion has shown improvement at times. Perhaps his statement is not reliable. It is possible also that it will later be discovered that erythroplasia may improve at times and that to some degree improvement may be spontaneous. The histologic picture is not that of erythroplasia, but perhaps a second biopsy will show an entirely different picture. At present I cannot subscribe to the diagnosis of erythroplasia, but certainly that possibility should be kept in mind. I am more inclined to consider a diagnosis of a fixed eruption due to a drug or of psoriasis.

DR. LUDWIG OULMANN: I should not consider the diagnosis of erythroplasia. In erythroplasia there is a fairly smooth surface and the process goes deeper, while the clinical picture in this case is a papillary structure due to dyskeratosis.

DR. ANDREW J. GILMOUR: I have nothing to add. My impression is that the disorder is psoriasis.

DR. ISADORE ROSEN: It is difficult to make a diagnosis after one examination of a disorder like this. On clinical grounds alone I should be inclined to agree with the members who believe that the condition is psoriasis. Psoriasis when it occurs on the glans penis does not as a rule show the same features as when it affects the trunk or other parts of the body. One of the reasons for the difficulty in making a diagnosis is the fact that the patient has received a great deal of treatment.

DR. J. FRANK FRASER: I can see no evidence of malignant degeneration in the section. The histologic picture suggests psoriasis.

DR. FRED WISE: I agree with the opinions expressed by Dr. MacKee. I believe that if the lesion were left alone for a week or two it would more nearly resemble psoriasis. It is quite possible that the whole histologic picture would change on an untreated area.

DR. GEORGE C. ANDREWS: The patient has consented to undergo another biopsy. The lesion did disappear, but that was after it was excised by the operation for circumcision. The patient says that the lesion has always been dry, but I have seen it when it was fairly moist. I shall follow Dr. Wise's advice and let it alone for a while and then make a biopsy.

A Case for Diagnosis (Duhring's Disease?). Presented by Dr. Paul E. Bechet.

E. M., a woman aged 46, a housewife, born in the United States, who is under the care of Dr. Mihran B. Parounagian, states that an eruption developed on the chest about seven weeks ago and later spread to the neck and face. The eruption appeared as large blisters; later reddening of the skin and formation of crusts developed. The patient has not been aware of any lesions in the mouth. There has been some burning of the skin in the affected areas, but there is no itching. The patient states that she has taken no drugs except compound effervescent powders U. S. P. and magnesium citrate.

The lesions are most marked on the anterior aspect of the chest and on the lateral and anterior aspects of the neck. There are scattered lesions on the face, and a few are present on the forearms, left thigh and auricles. The chief elements are bullae and crusted lesions, and considerable surrounding redness and inflammation of the skin are present. There are no lesions on the lips or in the mouth. The patient applied a 3 per cent ammoniated mercury ointment, which brought about only slight improvement; in fact new lesions (bullae) appeared. On January 6 a patch test with potassium iodide on the right forearm showed a strongly positive reaction, consisting of erythema with formation of vesicles. Almost at once after application of potassium iodide ointment the patient noted quite marked itching in the old lesions. The itching is still present. The Wassermann test was negative. The blood cell count showed 4,650,000 red cells, 12,100 white cells and 73 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclear neutrophils, 66 per cent; lymphocytes, 29 per cent; eosinophils, 5 per cent.

DISCUSSION

Dr. George M. MacKee: There is nothing about the eruption which to my mind suggests dermatitis herpetiformis. The striking features are the widespread erythema on the exposed areas of the chest, face and lobes of the ears and the numerous discrete bullae. In the absence of bullae one would consider the possibility of lupus erythematosus. The bullae, of course, suggest pemphigus provided an eruption due to a drug and erythema multiforme can be ruled out. I suggest the Senear-Usher syndrome as a possible diagnosis.

Dr. Andrew J. Gilmour: The eruption may have been affected by the cold weather or by the sun's rays, as it is located mostly on the surface exposed to the elements. I cannot suggest a diagnosis.

Dr. Max Scheer: I think that the eruption is due to exposure to light plus some added sensitizing factor or lupus erythematosus of the bullous type.

Dr. Paul E. Bechet: Dr. MacKee's suggestion is excellent. The eruption affects exposed parts of the body and there is a sharp line of demarcation; these features suggest the possibility that actinic light was an etiologic factor.

A Case for Diagnosis (Psoriasis? Mycosis Fungoides?). Presented by Dr. Fred Wise.

Mrs. F. V., a woman aged 50, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presented herself for treatment on Oct. 28, 1935, because of an eruption of about two months' duration. About fifteen years ago a scaly eruption appeared on the knees and elbows, remaining confined to these areas. This eruption subsided but reappeared in the same locations seven years ago and again two years ago; the last eruption has persisted to the present time. At present there is a widespread dermatitis involving the knees, elbows, trunk and scalp. On the upper and lower extremities, especially in the regions of the knees and elbows, are large scaly and crusted patches resembling psoriasis. On the trunk are widespread pink diffuse scaling areas in the midst of which are islands of uninvolved skin in the shape of irregular discoid formations. On the chest and back are scattered patches of infiltrated skin from 1 to 4 inches (2.5 to 10 cm.) in diameter which are slightly elevated, dark red

and somewhat scaly, resembling early lesions of mycosis fungoides. The lower portions of the ear lobes present a glistening, indurated and thickened dermatitis. The scalp is covered with adherent scales, the involvement being most pronounced anteriorly. The finger-nails are striated longitudinally but not pitted. Superimposed on these chronic lesions there is evidence of an acute diffuse follicular and scaly dermatitis evidently due to the recent use of some irritating topical remedies. The patient complains of intolerable itching and exhibits many marks of scratching. The Wassermann and Kahn tests were negative. The results of histologic examination will be reported at a subsequent meeting.

DISCUSSION

DR. MAX SCHEER: I think that the disease is mycosis fungoides. On the back there is an oval infiltrated lesion which resembles mycosis fungoides. Other lesions have changed as a result of treatment.

DR. ANDREW J. GILMOUR: I could not see any evidence of psoriasis, but I think that the diagnosis of mycosis fungoides is correct.

DR. ISADORE ROSEN: There is no question but that this patient has some lesions not unlike psoriasis, but there are also lesions scattered over the trunk which have features strongly suggestive of mycosis fungoides. Further studies and repeated histologic examinations will have to be made before a definite diagnosis can be arrived at.

DR. J. FRANK FRASER: I am inclined to favor the diagnosis of mycosis fungoides. There is a history of intense itching, and the clinical picture suggests the *homme rouge* type of that disease. Experience leads me to believe that a mutation from psoriasis to mycosis fungoides does not occur. In a patient who is still under observation the earliest clinical picture closely resembled that of psoriasis, and several members of this society subscribed to that diagnosis. Several biopsies were made, and the histologic picture supported the clinical diagnosis of psoriasis. Later when tumors developed and the microscopic picture became typical of mycosis fungoides a study was made of the sections obtained in an early stage of the disease on which the diagnosis of psoriasis had been based. In one field of one of these sections the typical reticulo-endothelial reaction with mitotic figures showed that the early clinical and histologic diagnoses were incorrect. The condition was mycosis fungoides all the time.

DR. GEORGE M. MACKEE: I doubt that there is ever a transformation of psoriasis into mycosis fungoides. It is well known that the prefungoid stages of granuloma fungoides may for months and years so closely resemble other diseases, such as parapsoriasis, psoriasis and different clinical varieties of eczema, that for long periods it is impossible to make the differentiation either clinically or histologically. The repeated discussions relative to this question can be applied to many dermatoses that at times closely simulate one another, namely, syphilis, tuberculosis, eczema, psoriasis, etc. As a matter of fact, clinical entities rest on rather insecure grounds. Often, indeed, their identities may be questioned. Dr. Wise's patient presents some lesions that suggest psoriasis, some that suggest mycosis fungoides and some that suggest eczema. For instance, the eruption on the knees resembles the variety of eczema known as neurodermatitis circumscripta, which is often difficult to differentiate clinically from psoriasis. It is possible, of course, for a patient to have more than one disease. It is possible that this patient has mycosis fungoides. If that is the case I believe that the disorder was mycosis fungoides from the beginning; I do not think that a change from psoriasis or eczema to mycosis fungoides has occurred.

DR. PAUL E. BECHET: The lesions on the knees are almost typical of neurodermatitis. There is a patch on the back which is sharply outlined and somewhat infiltrated. The diagnosis of mycosis fungoides should be considered. Dr. Fox reported one or two cases of psoriasis in which the manifestations remained typical of that disease for fifteen or twenty years and then developed into those of mycosis fungoides. I do not believe that a transition from psoriasis into

mycosis fungoides does occur. These disorders, though resembling psoriasis, are primarily atypical mycosis fungoides. In my opinion it is possible for mycosis fungoides to exist for many years without going on to tumor formation and to fatal termination, and in its early stages it frequently assumes the appearance of eczema or psoriasis with such success as to confuse the most astute observer.

DR. HOWARD FOX: The case to which Dr. Bechet referred was one which I reported. It was that of a man who for twenty-eight years had suffered from what appeared to be ordinary psoriasis and whose condition had been diagnosed as such by numerous dermatologists. When I saw him the eruption had changed and a clinical diagnosis of the infiltrative stage of mycosis fungoides was made. This was confirmed by histologic examination.

DR. FRED WISE: In this case one should be guarded in making the diagnosis of psoriasis, mycosis fungoides or a combination of both diseases. A histologic report will be submitted at a later date.

NOTE.—A subsequent microscopic examination revealed mycosis fungoides.

RECKLINGHAUSEN'S DISEASE. Presented by DR. PAUL E. BECHET.

L. N., aged 23, presented herself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 30, 1935, with an eruption of one year's duration. There are scattered lesions over the abdomen and back and isolated lesions on the arms. The lesions are pea-sized elevated soft and violaceous tumors. Digital compression causes them to disappear through a ring in the skin; release of the pressure causes a return to the normal elevated position. The patient presents no café au lait spots. The Wassermann and Kahn tests were negative. Urinalysis gave normal results. A biopsy of material from a lesion on the right arm revealed a microscopic picture typical of Recklinghausen's disease.

DISCUSSION

DR. FRED WISE: An interesting feature is the fact that the father of the patient had a number of café au lait spots on the body but no other lesions of Recklinghausen's disease.

SEBORRHEIC DERMATITIS AND FOLLICULITIS. Presented by DR. PAUL E. BECHET.

A. O., a woman aged 22, presented herself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 14, 1936, with an eruption involving the scalp, face, ears, axillae, region beneath the left breast, umbilicus, pubic area and groins. The eruption consists of numerous discrete and confluent erythematous patches, some of which are sharply marginated while others fade into normal skin. These patches are oozing. The lesions on the scalp are covered with an adherent greasy grayish white scale. The results of examination for tinea made today have not been reported. The patient was hospitalized at the Bellevue Hospital for one and a half months, at the Metropolitan Hospital for eleven months, at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for two months and at the New York City Hospital for one day. The patient states that she has a moderate vaginal discharge.

DISCUSSION

DR. FRED WISE: The only therapeutic suggestion I can offer is to paint the lesions with a 2 per cent solution of gentian violet.

DR. GEORGE M. MACKEE: Years ago I should have unhesitatingly made a diagnosis of seborrheic eczema. Now I am more careful. The inclination is to make the diagnosis of seborrheic eczema for the basic trouble complicated by the secondary variety of eczema known as infectious eczematoid dermatitis. However, I agree with Dr. Rosen that the diagnosis of moniliasis and that of the exudative type of psoriasis must be considered.

DR. PAUL E. BECHET: This condition is found as often in males as in females; this somehow tends to decrease the importance of vaginal organisms as a causative factor. My impression of this disorder is that the eruption begins as a typical seborrheic dermatitis in locations generally affected by seborrhea—the scalp, face, chest, axillae, umbilical and genital region—and that a secondary staphylococcia due to infection or lowered resistance on the part of the patient supervenes, the disorder thereby resulting in the typical weeping pustular dermatitis so commonly observed. This type of disorder is extremely resistant to treatment, and in dermatologic departments of hospitals there are always at least one or two patients with that condition. At rare intervals a plan of treatment almost effects a cure in a patient, and yet the same therapy has no effect whatever on another patient with a similar disorder.

A CASE FOR DIAGNOSIS (TOXIC MELANODERMA?). Presented by DR. MAX SCHEER.

J. Y., a woman aged 27, presented herself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 14, 1935, because of an eruption of thirteen years' duration. It was not accompanied by any subjective symptoms, and the patient applied for treatment only because she feared that other areas would become involved. The eruption is confined to the middle portion of the anterior aspect of the chest and to the back as far down as the lower part of the lumbar region. The primary lesion was a pinhead-sized pigmented macule which varied in color from light brown to dark brown. Pigmented spots of this kind dot the entire affected area and give it a mottled appearance. The skin between the spots is normal. Wassermann and Kahn tests were negative. The report on the histologic examination stated that the disorder fits in with the picture of toxic melanoderma as described by Riehl.

DISCUSSION

DR. MAX SCHEER: I do not believe that the disorder is Riehl's melanosis. There is no history of a dietary deficiency. Moreover, there are lesions on the covered parts of the body, a feature which is not found in Riehl's melanosis.

ERYTHEMA INDURATUM. Presented by DR. FRED WISE.

Mrs. J. O., aged 19, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presents an eruption on the lower aspect of both legs; the disorder is of three years' duration. On the lateral aspects of the right leg above the ankle and on the posterior aspect of the lower portion of the left leg the eruption consists of erythematous and violaceous roughly oval plaques with well defined borders. The skin appears to be glazed, slightly indurated and somewhat edematous. In the course of her work the patient frequently enters a butcher's icebox. The noteworthy feature because of which she is presented is the fact that tuberculin tests on Jan. 4, 1936, were negative with dilutions of 1:10,000, 1:100,000 and 1:1,000,000. Roentgenograms of the chest made on Jan. 11, 1936, showed no abnormalities.

DISCUSSION

DR. GEORGE M. MACKEE: I think that the disorder is typical Bazin's disease clinically. Histologically it may prove to be one of the closely allied conditions, such as so-called perivasculitis or periphlebitis nodularis.

LUPUS VULGARIS. Presented by DR. ISADORE ROSEN.

S. R., a man aged 34, presented himself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for treatment of an almond-sized erythematous infiltrated area on the lateral margin of the sole of the left foot of about fifteen years' duration. A biopsy made on Jan. 6, 1936,

showed typical lupus vulgaris. The patient also presents some scaling of the palms and soles. The culture was negative for the organism of tinea. The Wassermann and Kahn tests were negative.

RECURRENT RASH OF SECONDARY SYPHILIS. Presented by DR. ISADORE ROSEN.

H. H., aged 26, presented himself for treatment at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. The patient was exposed to infection in the last week of August 1935, and a lesion appeared on the glans penis on Sept. 10, 1935. He applied iodine locally for one week; then he went to a physician, who treated the lesion locally for a week and then made a blood test, the result of which was 4 plus. No dark field examination was made. There was swelling of the left inguinal glands. The patient was referred to a clinic, where he was found to have a roseola. He had no headache, sore throat, fever or pains in the joints. He was given one injection of arsphenamine at that clinic and was then referred to the Board of Health for further treatment. There he received twelve intravenous injections of arsphenamine followed by four intramuscular injections of a bismuth preparation. He then failed to present himself for treatment for one month. When he returned he received two more injections of arsphenamine, and thereafter he was treated at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. The roseola disappeared after the fourth injection of arsphenamine. The present eruption appeared immediately after the eighth injection of the first course, and the left arm became painful and swollen, remaining so for a week; a few days after the onset of the swelling the present itchy rash appeared on the whole body; it has persisted unchanged for the past seven weeks. Treatment was continued but had no influence on the rash.

DISCUSSION

DR. FRED WISE: My diagnosis of the cutaneous eruption is syphilis.

DR. MAX SCHEER: I think that the lesions are psoriasis. It might be worth while to try the *grattage methodique* advocated by Brocq.

DR. GEORGE M. MACKEE: In places the eruption suggests psoriasis; in other places it suggests syphilis. Configuration occurs in both conditions. The color in this case is more in favor of syphilis. The main point, however, is that the crusts represent ulceration and not the accumulation of scales so typical of psoriasis. Cases of this disorder were common years ago. The patient requires a continuation of antisyphilitic treatment judiciously administered, but he also needs building up and, perhaps, some fever therapy.

A CASE FOR DIAGNOSIS (SYPHILIS? PEMPHIGUS?). Presented by DR. ISADORE ROSEN.

A. I., a man aged 35, was born in Turkey. He has been married for eight years and has three children, the youngest of which is 14 months old. On admission he stated that he had a gonorrheal infection seventeen years ago. About five months ago, after he was exposed to infection, a lesion developed on the shaft of the penis. At that time his physician found that he had a positive Wassermann reaction and gave him five injections of arsphenamine—the dose was not stated—and five injections of a bismuth preparation. The patient presents an eruption on the forehead, face, chest, back, arms and legs. There are various types of lesions. On the forehead and face there are papular scaling lesions strongly suggestive of syphilis. On the chest and back the lesions are raised, being covered with heaped-up scales, and resemble either a rupioid syphiloderm or psoriasis ostreacea. Interspersed are grouped papulosquamous lesions which suggest secondary syphilis. On the arms and legs the lesions closely simulate psoriasis, although the elbows and knees are not involved. On the glans penis there are annular lesions, raised above the level of the skin, covered with a translucent scale and resembling those seen in keratosis blennorrhagica. There

is no generalized adenopathy, and repeated examinations from smears of the lesions failed to demonstrate spirochetes. The Wassermann test has been repeatedly negative. Biopsy showed a marked round cell infiltration around the blood vessels. The character of the inflammatory exudate in the corium was considered suggestive of syphilis. The patient has received arsphenamine and a bismuth preparation, but despite this therapy new lesions have appeared, and the older ones have not been influenced to any great extent.

DISCUSSION

DR. FRED WISE: I believe that the patient has pemphigus.

DR. GEORGE M. MACKEE: I think that the eruption is a syphilid for the reasons given in the discussion of the similar disorder in the other patient presented by Dr. Rosen.

DR. LUDWIG OULMANN: I am glad that Dr. Wise made a diagnosis of pemphigus. I asked Dr. Rosen whether he had made a Pels-Macht test. I agree with Dr. Wise.

DR. ANDREW J. GILMOUR: My diagnosis is syphilis.

A CASE FOR DIAGNOSIS (GRANULOMA ANNULARE [?] OF THE FACE RESEMBLING EPITHELIOMA). Presented by DR. GEORGE C. ANDREWS.

E. O., a man aged 40, is presented because of a lesion which began five years ago as a small papule on the left lower eyelid. He was a boxer at the time and received frequent blows on the eye. The lesion has never been tender. It has been treated with caustic remedies, but it has spread peripherally in spite of this. The patient has a fistula to the right of the anus. On the left lower eyelid there is an oval lesion with serpiginous outline, the periphery of which consists of a pearly ridge. The center is smooth and atrophic and shows some crusting. On the right cheek just below the eye there is a papule the size of a split pea, the consistency and color of which resemble those of the border of the lesion on the left lower eyelid.

NOTE.—A subsequent biopsy revealed basal cell epithelioma.

CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

Regular Meeting Jan. 15, 1936

DR. WILLIAM ALLEN PUSEY, *President, Presiding*

ATROPHODERMA WITH TELANGIECTASIA. Presented by DR. OLIVER S. ORMSBY.

This Polish woman, aged 56, presents a disorder of forty-six years' duration. She was presented before this society in 1928, 1929 and 1930 and before the American Dermatological Association in June 1933. A full description of the clinical symptoms, history and progress together with the results of histologic examinations is given in the ARCHIVES (**18**:306 [Aug.] 1928; **20**:388 [Sept.] 1929; **21**:666 [April] 1930; **29**:157 [Jan.] 1934).

The changes noted at present from the condition described in the last of the aforementioned references are as follows: On the face the skin shows no activity of the process and practically no sequelae. There are less scaling and less evidence of inflammation, but there is increased telangiectasia over the breasts. Over the anterior and posterior aspects of the trunk and over the arms there is less

scaling, but the wrinkling, atrophy and telangiectasia are unchanged. The ring of superficial pale red flat nodules situated above the knee has extended and developed into a plaque several inches in diameter. Itching continues in this plaque and in scattered areas elsewhere, but it is less severe and is greatly restricted in its distribution. There is no change in the general health.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: I have seen this patient on several occasions, and I believe that in the differential diagnosis idiopathic atrophy and poikiloderma atrophicans vasculare should be considered. While examining the patient I thought momentarily of the possibility, first called attention to by Dr. Otto Foerster, of the association of mycosis fungoides and poikiloderma. However, I believe that this patient presents an idiopathic atrophy of the skin.

DR. OLIVER S. ORMSBY: No new developments have occurred since June 1933, when the patient was presented before the American Dermatological Association. She has been seen by Professor Bloch and Professor Jadassohn and also by a number of the eminent dermatologists in this country, and her condition has not been definitely diagnosed. It is probably not an example of poikiloderma. The pruritus is unusual, and so is the extensive telangiectasia. The histologic picture closely resembles that of idiopathic atrophy. As previous investigation revealed no important findings, the disorder must still be classified as "atrophoderma with telangiectasia."

ANETODERMA ERYTHEMATODES, JADASSOHN (DERMATITIS ATROPHICANS MACULOSA WITH BALLOONING). Presented by DR. O. H. FOERSTER, Milwaukee, DR. H. R. FOERSTER, Milwaukee, and DR. LESTER M. WIEDER, Milwaukee.

L. J., a boy aged 12 years, is presented because of a cutaneous eruption not associated with systemic symptoms which was first observed in December 1934 and which has steadily increased. The lesions are symmetrically distributed over the upper portion of the chest and back; they do not extend below the transverse nipple line anteriorly or below the lower borders of the scapulae posteriorly and do not involve areas above the jaws and above the hair line. There are a few lesions on the upper extremities, but most of the eruption occurs on the upper portion of the chest and on the posterior aspect of the shoulders.

The lesions are pink to red round or oval macules varying in diameter from 2 mm. to 2 cm.; some older lesions exhibit a grayish cast. The smallest and earliest lesions are slightly raised infiltrated red maculopapules showing exaggerated surface markings; the largest are dull pink macules with a wrinkled atrophic surface. Many of the latter lesions exhibit a domelike elevation which is easily invaginated by pressure and "balloons" when pressure is released.

There is an abnormal development of adipose tissue, particularly of the breasts, hips and thighs. The mother states that the boy developed rapidly after the eighth year, putting on an excess of weight—he now weighs 115 pounds (52 Kg.)—and that he exhibited stiffness and physical lethargy at play. There has been a recent disability of the left hip. Mental development is apparently normal.

He has had headache almost daily since childhood; the headache is particularly severe and is associated with vomiting when meals are delayed. Because an endocrine factor, possibly pituitary involvement, was suspected, it was suggested that the patient undergo a complete clinical and laboratory investgation, and he was advised to go to the Mayo Clinic.

The following findings were recorded at the Mayo Clinic: The metabolic rate was —22 per cent; roentgenograms of the chest and skull showed no abnormalities; examination of the urine, a tuberculin test and a serologic test for syphilis gave negative results. Examination of the blood showed 4,350,000 erythrocytes, 11,300 leukocytes and 92 per cent hemoglobin. The results of the differential count were as follows: neutrophils, 65 per cent; eosinophils, 25 per cent;

lymphocytes, 25 per cent; monocytes, 7 per cent. Studies of the chemical composition of the blood were not made. The orthopedic department diagnosed the condition in the hip as "slipped epiphysis." Dr. Montgomery and a pediatrician saw the patient, and Dr. Montgomery suggested the possibility that the cutaneous condition represented multiple benign tumor-like new growths of the Schweninger and Buzzi type or an abortive form of Recklinghausen's disease; after studying sections subsequently submitted to him he expressed the opinion that the histologic picture was consistent with that of the former disease.

The histologic section of an intermediate lesion studied by my co-workers and me showed atrophy of all the layers of the epidermis, condensation and some fragmentation of the collagen, atrophy of the cutaneous glands and narrowing of subpapillary vessels, with moderate infiltration of round endothelioid cells about the vessels. The elastic tissue was absent in the center of the lesion; in other areas it was reduced and fragmented.

DISCUSSION

Dr. William Allen Pusey: This condition, I think, belongs in the group of disorders of which I presented the first American example several years ago with the diagnosis of multiple benign tumor-like new growths of the skin of the Schweninger and Buzzi type. In my case I regarded the disorder as a congenital defect in the skin; there was great thinning in the corium, which resulted in ballooning of the subcutaneous tissue through the weak spots in the corium. It is not surprising that other congenital defects of the skin should occur in association with such weak spots.

Dr. Hamilton Montgomery, Rochester, Minn.: At the Mayo Clinic my co-workers and I have observed a number of cases of Recklinghausen's disease in which varying numbers of lesions have presented the features of ballooning. Histologically this was proved to be due to the destruction of the elastic tissue. I think that Recklinghausen's disease and multiple benign tumor-like new growths of the Schweninger and Buzzi type are closely allied and may even be variants of the same process.

Dr. Richard S. Weiss, St. Louis: Have roentgenograms been made of the skull, particularly with reference to the condition of the frontal bone? Dr. Sherwood Moore described a syndrome under the name of hyperostosis frontalis interna *(Surg., Gynec. & Obst.* **61**:345 [Sept.] 1935); this boy seems to present some symptoms that led me to think that he may be suffering from that condition. Headaches and a peculiar type of obesity are associated with the syndrome, and it would be interesting to investigate the patient from this standpoint.

Dr. Oliver S. Ormsby: When patients with this condition were first seen they were thought to have Recklinghausen's disease, but I think now that their disorder is considered a disease per se.

Dr. Ruben Nomland: I think that this boy presents symptoms that are usually known as anetoderma erythematodes of Jadassohn. The early atrophic lesions are red, which is usually not the case in macular atrophy. Dr. Ebert recently called attention to the fact that red atrophic striae occur in women who have not been pregnant and even in males. His patients with atrophic striae apparently had an endocrine dysfunction. It is probable that this boy has an analogous syndrome but that the reaction occurred in macules and not in striae.

Dr. H. R. Foerster, Milwaukee: The lesions at their onset are small and definitely infiltrated, but they rapidly become atrophic as they enlarge, and they are inflammatory throughout. There have been no linear lesions and no striae distensae. We believe this condition to be similar to Jadassohn's anetoderma erythematodes, which in his textbook Dr. Ormsby classifies under macular atrophies. In our case we excluded the Schweninger-Buzzi syndrome because of the absence of infiltration and because of the inflammatory character of the fully developed lesions. The lesions in the Schweninger-Buzzi syndrome are described as slate gray and as exhibiting palpable infiltration. We believe that this patient has an

endocrine disorder, possibly involvement of the pituitary gland, and that the cutaneous lesions are only one feature of his disease, which may be Fröhlich's syndrome.

ONYCHOLYSIS. Presented by DR. F. E. SENEAR.

This girl, aged 9 years, about one year ago, without having exhibited any preceding inflammatory reaction, shed a toe-nail. The nail regrew and was of normal appearance. Later one finger-nail behaved similarly, and since then the mother has noted discoloration of four finger-nails associated with separation of the plate from the bed.

When the patient was seen in November 1935 the nails of the left great toe and left second toe were yellow and friable. The nails of the ring finger of the right hand and of the two outer fingers of the left hand showed separation from the bed. The plates were smooth, and one of them was of typical egg-shell color.

DISCUSSION

DR. H. R. FOERSTER, Milwaukee: Dr. Everett Fox, of Dallas, Texas, has observed a number of cases of separation of nails from the nail bed and loss of nails, in all of which he noted hypothyroidism. Normal growth of the nails is said to have followed the administration of thyroid extract.

DR. WILLIAM ALLEN PUSEY: It is interesting to see patients with these disorders, and it is only by studying such disorders that one can hope to get some real information about them. At present there exists a state of confusion regarding all these disorders of the nails.

INOCULATION TUBERCULOSIS WITH SCROFULODERMA. Presented by DR. S. W. BECKER.

This boy, aged 4 years, noted a "wart" on the right heel three months ago. A little pus could be expressed from the lesion. A few days later red streaks were noted on the leg, and the lesion on the heel was incised by a physician. A swelling was noticed in the femoral region, and the incised wound drained a small amount of pus. On the median side of the right heel was a nonelevated slightly erythematous rough lesion about 1 cm. in diameter. In the right femoral region were two swellings of about the same size, one of which was draining purulent material.

Culture of material from the femoral region, which had not yet broken down although it was fluctuant, showed Staphylococcus albus. Inoculation of guinea-pigs gave positive results for acid-fast bacilli.

A section removed from the lesion on the heel showed numerous tubercles with large giant cells.

An intradermal test with a 1:100,000 dilution of old tuberculin gave a positive reaction on the right arm.

DISCUSSION

DR. HENRY E. MICHELSON, Minneapolis: This patient is presented with a diagnosis of inoculation tuberculosis with scrofuloderma. If one accepts the findings in their component parts I quite agree with the diagnosis, but I should like to consider the lesion on the foot and that on the groin together and call the entire picture a primary tuberculous complex of the skin. I think that the child had an implantation of tubercle bacilli on the foot, and probably he was free from tuberculosis at the time of the implantation. It is of course impossible to know what the reaction to tuberculin was at the time of inoculation. The infection spread by way of the lymphatics, and at the glandular barrier a new reaction was set up, which has erupted through the skin. Even though the child is now examined for tuberculosis with the most scrupulous care, it is possible that a primary pulmonary complex has been present, but it cannot be demonstrated with roentgen rays unless the glands have become calcified. My conception of the primary complex of tuberculosis in the skin is an implantation of infection into the skin of a subject free

from tuberculosis resulting in the development of a lesion at the site of implantation and subsequent involvement of the regional glands.

The treatment should be that used for tuberculosis, and locally the lesions may be treated with heat or roentgen rays, and the glands may be treated in a like manner or excised. The tendency of the lesion at the site of inoculation is to heal. Healing of the glandular lesion is much slower. The prognosis, provided reasonable treatment is given, is good.

Dr. Oliver S. Ormsby: I presume Dr. Michelson refers to the type of lesion which English authors have called a tuberculous chancre and which is now termed a primary complex. My co-workers and I observed such a lesion in a girl about 16 years old who had been seen for other conditions. She presented a lesion simulating a chancre on the brow near the inner canthus and had enlarged glands in the neck. A short time later Professor Bloch saw her. He definitely considered the lesion a primary complex. He brought up the point that the lesion might not be a primary chancre but might be a metastasis from an internal focus. The patient has been under observation for several years, and a roentgenogram of the chest has revealed no signs of tuberculosis. She recovered without exhibiting further lesions, and the primary lesion disappeared as a result of roentgen therapy.

Dr. Paul A. O'Leary, Rochester, Minn.: Dr. Michelson and I have discussed the problem presented by this child on several occasions before the Minnesota Dermatological Society. Our ideas differ on the interpretation of the term primary complex. I prefer the term inoculation tuberculosis for this characteristic tuberculous chancre and bubo to which Stokes called attention ten years ago. The advocates of the term primary complex attach great significance to the presence of a negative reaction to tuberculin before the appearance of the tuberculous chancre, a finding which, I believe, is too variable to be the essential feature in the diagnosis of inoculation tuberculosis. However, I agree that the chancre is a primary infection in a person who does not have tuberculosis and has a good defensive reaction to the disease. I have for several years endeavored to prove that the bovine or the avian type of the tubercle bacillus was the cause of this pathologic entity, but I have not been successful thus far. In my experience when the primary lesion and the bubo have been excised—a procedure which I have followed in the majority of cases which have come under my observation—recurrences or metastases have not occurred.

Dr. Hamilton Montgomery, Rochester, Minn.: At the Mayo Clinic there recently was a patient, a child, who presented a true primary cutaneous tuberculous complex. She had a mosquito bite on the cheek; this became infected and presented an ecthymatiform appearance, and the adjacent glands in the neck became enlarged. Roentgenograms of the chest showed no evidence of tuberculosis, and the tuberculin test was negative at the time of the initial examination. Two weeks later the tuberculin test was positive, and the gland had broken down. Biopsy revealed a nonspecific type of infiltrate in one area with many bacilli, and adjacent thereto early tubercle formation with epithelioid cells and a few giant cells; in the latter area no tubercle bacilli were present. In this case all the criteria for a primary cutaneous tuberculous complex were present, and I think that if Dr. Becker had had the opportunity of examining his patient early enough in the course of the disease he would have found first a negative and later a positive reaction to tuberculin.

In contrast, my co-workers and I have observed other cases of inoculation tuberculosis, generally in older persons, in which we could not be sure whether or not the patients had tuberculosis before the symptoms appeared. In those cases the primary chancre early reveals the specific tubercle formation histologically and shows the apple jelly nodules clinically. This type of lesion is often seen in farmers and veterinarians; possibly it is due to external infection with avian or bovine tuberculosis.

All types of tuberculosis in the fully developed stage reveal specific tubercle formation, both in the primary chancre and in the adjacent glands, and marked caseation necrosis.

DR. S. W. BECKER: When this child was first seen the original lesion on the heel had practically healed and there was fluctuation in the femoral node. The patient was on the surgical service and was seen in consultation, and I suggested the possibility of tuberculosis. A few weeks later she was brought back with inflammation in the primary lesion and apparent extension of the process in the groin. When a section for biopsy was taken the whole lesion was cauterized because it was convenient to perform the operation at that time. My co-workers and I are planning to excise the glands, although, as Dr. Michelson stated, there is a possibility of tuberculous infection in the wound.

SCLERODERMA; SCLERODACTYLIA. Presented by DR. OLIVER S. ORMSBY.

This girl, aged 5 years, presents a disorder of eight months' duration. The first symptom noted was stiffness of the fingers. When this was noted the child was examined, and it was found that the texture of the skin of the forearm felt abnormal and that there was a thickened spot on the chest. Within a month other areas of depigmentation were noticed.

The right arm and right side of the face are somewhat smaller than the left. The last three fingers of the right hand are fixed in flexion, firm to the touch, waxy white and somewhat smaller than normal. There is a definite firmness palpable in the subcutaneous tissues and muscles of the right forearm, and similar changes are found in the external aspect of the right lower extremity. An ivory-colored plaque measuring approximately 2 by 6 cm. involves the entire thickness of the skin of the medial surface of the right biceps. There is a similar plaque measuring 1 by 2 cm. over the sternum, and a somewhat smaller lesion is located over the right temple. An elongated plaque of this type runs beneath the ramus of the right jaw. There is a mottled depigmentation on the right side of the body; it is most noticeable over the medial surface of the right arm and on the right side of the chest and right flank, extending down the right lower extremity. The same type of depigmentation extends across the hips to the left side. A similar change is noticeable about the umbilicus. The remaining skin of the trunk seems to exhibit a slight degree of hyperpigmentation.

DISCUSSION

DR. PAUL A. O'LEARY: Rochester, Minn.: I had the opportunity to examine this child two weeks ago, and I believe that her disorder belongs in the group of hemiatrophy rather than in that of scleroderma per se. My reason for this distinction is that this condition apparently develops as the result of cerebral injury caused either by infection or by trauma, which in turn produces the sclerodermatous plaques or bands. In several of my cases a cervical and lumbar sympathectomy has been performed on the involved side without great benefit. The purpose in subjecting children with this disorder to such a radical surgical procedure is to prevent, if possible, the severe osseous deformities that develop on the involved side rather than to try to influence the scleroderma. The scleroderma tends to involute while the bones and other structures on the involved side cease to grow.

DR. OLIVER S. ORMSBY: As to terminology, I agree that Dr. O'Leary's description is correct. I have seen a number of children with superficial sclerodermatous lesions on the trunk, but none had this peculiar sclerodactylia-like involvement of the hand.

PSEUDOXANTHOMA ELASTICUM (DARIER) ASSOCIATED WITH FORMATION OF BONE. Presented by DR. B. B. BEESON.

This woman, aged 52, states that her cutaneous trouble has been present for ten years. A general physical examination gave essentially negative results.

The skin is relaxed and hangs in folds about the neck, axillae, abdomen and thighs. There appears to be a network of yellowish papules, which are, however, not elevated.

Microscopic examination revealed clumping and swelling of the elastic fibers. Bony formation and calcification were present, the groundwork of some of the calcified areas being composed of interwoven elastic fibers. The sections were examined by Dr. Jaffé and Dr. Civatte, both of whom observed the formation of bone.

DISCUSSION

DR. CLARK W. FINNERUD: At a previous meeting Dr. Nomland and I presented a patient with pseudoxanthoma elasticum, and we have been studying the case from the standpoint of the calcium content of the elastic tissue. Since that time we have studied another case of that condition. In view of the fact that there is no specific stain for calcium, hematoxylin being as good as any other stain, we decided to measure quantitatively the amount of calcium in tissue affected with pseudoxanthoma. We have found that whereas in normal skin the calcium content is approximately 1 per cent, in these two cases it was 5 and 6 per cent. Apparently in cases of pseudoxanthoma elasticum most of the calcium is deposited in the elastic tissue. This may also be true of other similar conditions that have not yet been studied. I think there is no question about the diagnosis. This is not formation of bone, as stated by Dr. Beeson, but marked deposition of calcium in the degenerated elastic tissue.

DR. O. H. FOERSTER, Milwaukee: It is interesting that this patient, who presents an extensive example of the disorder, was said not to show the angioid streaks. A patient recently seen by us, in whom the condition has certainly existed no longer than six months, definitely showed angioid streaks.

DR. CLARK W. FINNERUD: In our series my co-workers and I are reporting a case of pseudoxanthoma with angioid streaks, one of pseudoxanthoma without the streaks and one of angioid streaks without pseudoxanthoma elasticum.

DR. B. B. BEESON: The most extensive review of this disorder is that by Surmont. In his series of about thirty cases, calcification was present in three.

ERYTHEMA AB IGNE. Presented by DR. E. A. OLIVER.

This white woman, aged 24, for the past four years has complained of dryness and scaliness of the skin of the eyelids accompanied by an eruption of styes.

She has been treated at various times with hot compresses of boric acid and with radiant heat.

The skin of both upper eyelids is mottled, showing a light brown reticulated pigmented erythema; the reticulation is quite marked.

DISCUSSION

DR. HENRY E. MICHELSON, Minneapolis: I believe that a biopsy should be made. My clinical diagnosis is lichen planus but of course that would have to be verified by a microscopic examination. I recently saw a patient who had a residual melasmic staining confined to the eyelids which on section proved to be lichen planus. The rest of the body was completely clear.

DR. OLIVER S. ORMSBY: What application of heat was made?

DR. CLARK W. FINNERUD: I wonder whether the hyperpigmentation was not accentuated by the absorption of the ammoniated mercury which was used?

DR. E. A. OLIVER: The patient is now using an ointment containing yellow mercuric oxide locally and is taking quinine. Several years ago she was treated by an ophthalmologist for recurrent styes. While she was in the hospital hot compresses of boric acid were applied to the lids, and she received radiant heat. I admit that I did not consider the diagnosis of lichen planus. Dr. Senear saw the patient with me several times, and as he presented one of the first cases of lichen planus of the eyelids before this society he naturally would have considered that possibility. Dr. Senear and I believe that this is a clearcut case of erythema ab igne.

DR. OLIVER S. ORMSBY: I knew Dr. Oliver was going to present a patient with this diagnosis, and in view of the fact that this disorder is supposed to be produced by fire I wish to show a photograph of a perfectly classic erythema ab igne with pigmentation following hot applications in a patient with herpes zoster.

LIVEDO RETICULARIS. Presented by DR. M. H. EBERT.

This woman, aged 40, presents a bluish red reticulation over the extensor surfaces of the arms and forearms, the dorsa of the hands, the calves and the buttocks; there is also a slight involvement of the scapulae. The eruption presents the same pattern as cutis marmorata but it is more violaceous and does not disappear when the body is warm or during the summer. The color disappears on pressure with the diascope but returns slowly. There is no palpable infiltrate in the lesions. They cause no sensation. The patient has a chilblain circulation of the hands, feet and nose. Her sister has a similar pattern of cutis marmorata, which is transitory and appears only when she is chilled. The patient's eruption appeared ten years ago, two years after she started to work in a fruit store where the atmosphere was always cold and damp. Her father became paralyzed when he was in his forties. The patient has been married for several years but has never been pregnant. There is no evidence of syphilitic infection.

A series of injections of neoarsphenamine had no effect on the skin. Repeated Wassermann tests have been negative. The patient exhibited a negative reaction to an injection of full strength of a purified protein derivative of tuberculin. Her basal metabolic rate when she was first seen, over a year ago, was —12 per cent. It was brought up to normal by the administration of thyroid, but this had no effect on the disorder. Her blood pressure has varied from 140 to 160 systolic and from 90 to 100 diastolic. Her only additional complaint is nervousness.

DISCUSSION

DR. M. H. EBERT: I did not have the opportunity in presenting the patient to state that the Wassermann reaction was negative and that the result of injection of arsphenamine is negative so far as the lesions are concerned. The tuberculin test was also negative, and roentgenograms of the chest showed no abnormalities; hence two most common causes of livedo, i. e., syphilis and tuberculosis, are ruled out. Cases have been reported in which the livedo reticularis was associated with arteriosclerosis, and others in which it occurred in association with what is called an anomaly of the blood vessels. This woman presents no evidence of arteriosclerosis, except a slight elevation of the blood pressure, the systolic pressure being from 150 to 160. Her father died of apoplexy when in his early forties. Her sister has a similar cutaneous condition.

Erythema ab igne has the same anatomic basis as livedo reticularis, i. e., a slowed-up circulation producing this peculiar pattern.

CREEPING ERUPTION. Presented by DR. RUBEN NOMLAND.

This man, aged 28, states that he acquired his disorder in Bermuda two months ago. It originally manifested itself as itching lesions on the scrotum and thighs which appeared after the patient had spent only a few hours on the beach. In its progress one of the lesions on the left thigh moved at least 8 inches (20 cm.) in a straight line, and probably twice as much in all, from the point of its origin. Within the past four days it has progressed more than 1 inch (2.5 cm.).

There are many inflammatory vesiculopapules on the scrotum and several lesions on each thigh. Several active burrows—circuitous red lines ending in a vesicle—can be seen running along the thighs for a distance of from 1 to 6 cm.

DISCUSSION

DR. OLIVER S. ORMSBY: For several years this disorder was considered rare. One or two cases of it were observed in Philadelphia. I had never observed one,

but Dr. Kirby-Smith reported a series of two or three hundred. The disorder is comparatively common in the southern and southwestern parts of this country.

Dr. William Allen Pusey: I can confirm what Dr. Ormsby has just said. I spoke to Dr. Kirby-Smith recently, and he told me that in Florida the disorder is not rare. The larva which causes the condition was first pictured by a Russian in a free hand drawing, but no one else has been able to recover the organism. It was so long before any one could locate it that his observation was impugned. When I was writing the first or second edition of my textbook on dermatology I received a letter from a country physician in Montana who said that he had observed one case of creeping eruption in which a lesion progressed right across the eyelid and that he had recovered the organism. He sent me photomicrographs of the organism which exactly duplicated the drawing made by the original observer. As far as I know, this physician was the first in this country to recover the larva.

Dr. Ruben Nomland: The members probably know that Dr. Bedford Shelmire studied this disorder and proved that the creeping eruption which occurs in the South is caused by the larva of the hookworm which infests cats. (Shelmire, Bedford: Experimental Creeping Eruption from a Cat and Dog Hookworm [A. Braziliense], *J. A. M. A.* **91**:938 [Sept. 29] 1928.)

Superficial Epithelioma. Presented by Dr. M. H. Ebert.

This man, aged 64, presents an eruption on the upper portion of his left leg which, he states, appeared thirteen years ago as a small rough spot which gradually enlarged. It has caused him no inconvenience.

There is a dollar-sized plaque with a slightly elevated dull red border made up of small nodules. The center is slightly depressed, atrophic and deeply pigmented.

Histologic examination of tissue from the margin disclosed a superficial basal cell epithelioma.

Xanthoma Multiplex. Presented by Dr. T. K. Lawless.

This infant, aged 5 months, at birth was free from all manifestations of cutaneous disorder. A week or ten days later there appeared on the head and face an eruption consisting of pale yellow to yellowish brown papules and nodules of various sizes and shapes. The lesions were firm and painless on pressure. The entire picture was progressive, both as to the areas involved and as to the size of the lesions. There is no history of diabetes or disease of the gallbladder in the family, although during the past two years the child's father has been incapacitated because of glomerulonephritis.

The histologic picture is typical of xanthoma. The results of chemical examinations of the blood are shown in the tabulation.

	Mg. per 100 Cc. of Plasma		
	First Determination 1/15/36	Second Determination 1/31/36	Normal Values (Adult)
Total cholesterol (Bloor's saponification method)	104	83.3	150 —190
Lipoid phosphorus	10.3	11.3	7 — 14
Lipoid lecithin	259	282.9	175 —330
Total cholesterol (Okey's digitonin method)	80.6	98.25	135 —120
Free cholesterol	31.35	31.35	40.5—103
Total fatty acids (Bloor's method)	473.55	361.9	290 —420

DISCUSSION

Dr. Clark W. Finnerud: I know that several other members think, as I thought in the beginning, that the disorder is urticaria pigmentosa with xanthoma-like lesions, but there was no urtication, and the sections ruled out that diagnosis. I also thought of nevoxantho-endothelioma, but I think that the sections ruled out that diagnosis also. I think that this disorder is of the type described, chiefly

by Artz, as juvenile xanthoma. In the disorder which he described the histologic picture was essentially identical with that in this case. The sections contained a large number of multinucleated giant cells.

PURPURA WITH ANNULAR LESIONS. Presented by DR. E. P. ZEISLER.

This white woman, aged 40, presents a purpuric eruption of two weeks' duration on the lower extremities and lower portion of the abdomen. She states that she had taken iodides before this eruption appeared and that she also used feenamint. The urine at one time showed sugar, but it has been normal recently.

Examination of the blood gave normal results. Some of the lesions have enlarged and involuted to form annular purpuric patches.

DISCUSSION

DR. HENRY E. MICHELSON, Minneapolis: I venture the diagnosis of purpuric pigmented lichenoid dermatitis. I realize the danger of making this diagnosis, for the knowledge regarding this condition is not complete. My opinion is that in most instances the individual lesions look like Schamberg's disease, and the proportion of purpuric punctae, papular lesions and pigmentation varies considerably. I believe that whatever causes the trouble affects the blood vessels and allows extravasation with a varying degree of infiltration. Since I have become interested in this subject I have seen a number of cases, and in most of them the eruption begins to fade in the center of the plaque and gradually disappears completely. I believe that the condition exhibited by Dr. Zeisler's patient can be classed under this heading.

DR. RICHARD S. WEISS, St. Louis: This patient states that she took potassium iodide. I have seen several patients who exhibited a purpuric eruption following the use of potassium iodide, and I wonder whether or not this drug has played a part in causing this patient's eruption.

DR. E. P. ZEISLER: I am glad to hear Dr. Michelson's remarks. I thought it best to present the patient without committing myself as to the type of purpura. Whether purpuric lichenoid dermatitis is to be classified as a distinct clinical entity has not been decided, and it will probably remain an open question, at least until further clinical reports are available.

THE FOX-FORDYCE DISEASE. Presented by DR. E. A. OLIVER.

This Negress, aged 43, who was treated for syphilis at the clinic of St. Luke's Hospital during the past three months has complained of an annoying pruritic papular eruption in both axillae.

In both axillary fossae there are discrete papules, from the size of a pinhead to that of a small lentil; they are sharply defined and are present in rather large numbers. There are no lesions in the pubic region.

DISCUSSION

DR. E. A. OLIVER: I hoped this presentation would bring forth some discussion, for I do not know how commonly the Fox-Fordyce disease occurs in Negroes.

DR. RICHARD S. WEISS, St. Louis: I have seen three cases of Fox-Fordyce disease in Negroes.

DR. F. E. SENEAR: About five or six years ago a Negress with the Fox-Fordyce disease was presented before this society (ARCH. DERMAT. & SYPH. **18**:788 [Nov.] 1928). That patient was unusually intelligent and temperamentally was the kind of person in whom that disease is apt to occur. Later I learned from Dr. Weiss that the disease occurs in Negroes.

DR. S. W. BECKER: I had occasion recently to review some work regarding the skin of Negroes, and I came across the statement that the apocrine glands, the involvement of which is characteristic for the Fox-Fordyce disease, are about three times as numerous in Negroes as in white persons.

A Case for Diagnosis (Multiple Idiopathic Hemorrhagic Sarcoma [Kaposi]?).
Presented by Dr. F. E. Senear, Dr. M. R. Caro and Dr. Earl R. Pace.

This girl, aged 18, was presented before this society in October 1932 (Arch. Dermat. & Syph. **27**:851, [May] 1933). The lesions had appeared two weeks previously following a dislocation of the right ankle.

During the past three years, in spite of considerable roentgen therapy, the lesions have continued to extend; at present they involve both sides of the right ankle.

A Case for Diagnosis (Idiopathic Multiple Hemorrhagic Sarcoma [Kaposi?]).
Presented by Dr. Theodore Cornbleet and Dr. Earl R. Pace.

This man, aged 26, an American of Polish descent, first noted a tender "pimple" on the lower portion of the right leg. He presented himself at the clinic of the Cook County Hospital in August 1935, exhibiting a dusky red lesion the size of a half palm above the external malleolus, at about one-third the distance to the knee. The lesion lacked infiltration at that time, except near the center, where it was somewhat elevated and presented a small, crusted, granulomatous area which appeared to be an indolent pyogenic ulcer. Antiseptic local applications seemed only to free it of pustular discharge. In September it was noted that the entire patch was becoming infiltrated, that it was rather sharply marginated and that very little of the color was removed by pressure with the diascope.

The results of a biopsy made in September 1935 were reported by Dr. Caro as follows: The epidermis showed a thin, non-nucleated scale, acanthosis of the rete mucosum, a thickened granular layer and an intact basal layer. The papillary and subpapillary layers of the corium showed proliferation of young blood vessels surrounded by a diffuse infiltration of histiocytes, much brown pigment—which occurred free and within cells—and many extravasated erythrocytes. Chromatophores were present about the deeper blood vessels and were scattered diffusely through the corium. Staining for iron showed dense deposits of hemosiderin in the upper part of the corium and about the deeper blood vessels and sweat glands and a smaller amount scattered throughout the tissue.

During November and the early part of December the patient received intensive roentgen therapy, and during the past seven weeks he was ordered to remain in bed so as to remove any elements of stasis. The lesion has lost most of its infiltration, but it has extended somewhat, and the color remains about the same.

The results of a biopsy made at the Cook County Hospital on Dec. 2, 1935, were reported as follows: There is capillary angiomatosis of the entire cutis, with extension into the subcutaneous tissue and marked deposits of blood pigment. The covering epidermis shows acanthosis and hyperkeratosis.

DISCUSSION

Dr. F. E. Senear: The young woman presented has large ulcerating lesions on the outer aspect of the ankle. We had not thought of Kaposi's sarcoma as the diagnosis, but the section, as Dr. Caro saw it, indicated that disorder at the time the patient was presented before the society, and, as I remember, Dr. Michelson and Dr. Montgomery agreed with the pathologic diagnosis, but Dr. Finnerud did not. The patient was given roentgen therapy. The lesions on the outer side of the right ankle have not extended, and the ulceration and vegetative character have been considerably reduced. The lesion on the inner aspect of the ankle has ulcerated.

The second patient was seen at the Cook County Hospital by Dr. Cornbleet and Dr. Pace, and the picture he presents is similar to that exhibited by the young woman. Neither of the patients presents manifestations which we regard as signs of Kaposi's sarcoma, and the patients are presented not with that diagnosis but rather as exhibiting a pathologic picture which apparently is compatible with a diagnosis of Kaposi's sarcoma.

Dr. Clark W. Finnerud: I believe that in the young woman there is a chronic hypostatic process, an old lichenified patch on one side and what amounts to a varicose ulceration on the other. A chronic hypostatic condition like this is not

uncommonly responsible for extravasation of blood pigment, which histologically is present in the cutis, and also for the change in the blood vessels. The picture in the young man is somewhat similar. I believe that the young woman does not have Kaposi's sarcoma, and I am not at all sure that the man has.

PEMPHIGUS OF THE SENEAR-USHER TYPE WITH ORAL LESIONS. Presented by DR. E. P. ZEISLER.

This man, aged 50, has had for seven years recurring bullous lesions in the mouth and on different areas of the body, chiefly on the chest, back, axilla and groin and in the anal region. The involvement in the mouth is acute; the lesions are painful and soon become covered with a pseudodiphtheritic membrane. The cutaneous bullae at present are few and have become crusted. Those around the anus have assumed a vegetating character. There has been no appreciable loss of weight, and there are no marked constitutional symptoms.

A recent examination of the blood showed 5,010,000 erythrocytes, 7,000 leukocytes and 80 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclears, 74 per cent; lymphocytes, 20 per cent; monocytes, 1 per cent; eosinophils, 2 per cent, and basophils, 3 per cent. Smears from the mouth showed diphtheroids, streptococci, a few Vincent bacilli and no Monilia.

Treatment has consisted chiefly of administration of various forms of arsenic and of tryparsamide. Recently there has been some improvement as a result of oral administration of acetarsone.

The patient was formerly under Dr. Oliver's care, who presented him before this society four years ago (ARCH. DERMAT. & SYPH. **23**:995 [May] 1931).

The patient has also recently taken some tablets of erythrol tetra-nitrate in doses of ½ grain (0.0324 Gm.) with some benefit.

DISCUSSION

DR. E. A. OLIVER: I disagree with the diagnosis of pemphigus of the Senear-Usher type. I believe that the disorder is pemphigus vulgaris. I presented this man before this society about five years ago with the diagnosis of pemphigus of the mucous membranes. He was under my care for about a year, and during that time was given the Davis treatment and injections of tryparsamide. In July 1935 he returned; at that time his mouth was badly involved and he had lesions on the body. For about three months he took one-half grain of erythrol tetra-nitrate twice daily. This, I believe, helped him considerably.

DR. RICHARD S. WEISS, St. Louis: Erythrol tetra-nitrate has been suggested by Dr. Cyril McBryde as a remedy for pruritus. It was used especially in the treatment of dermatitis herpetiformis and of the pruritus associated with jaundice, and some good results were obtained, but I have not heard of its being used in treatment of pemphigus. The improvement of pemphigus by the Davis treatment, I believe, is due to the arsenic rather than to the coagulating preparation used. In a certain percentage of the cases if sufficient arsenic can be introduced into the system, improvement and sometimes cure results. Pollitzer's solution, consisting of sodium arsenate, 1 Gm., phenol, 1 Gm. and distilled water, 50 cc., injected intramuscularly in doses of 1 cc. daily or every other day seems to be as efficient as iron cacodylate. Other forms of arsenic, such as tryparsamide, may also give good results. I have had one patient, as Dr. Ormsby and Dr. O'Leary may recall, a woman with a severe pemphigus vegetans, who recovered completely after taking huge doses of viosterol by mouth and has remained well over a period of about three years.

DR. E. P. ZEISLER: I am glad to hear Dr. Oliver dispute my diagnosis. I am always reluctant to make a diagnosis of the Senear-Usher type of pemphigus, but the long duration of the disorder in this case does not fit in with the duration in most cases of pemphigus, and I thought that the relatively benign course might justify the diagnosis pemphigus of the Senear-Usher type. At about the same time Dr. Oliver prescribed erythrol tetra-nitrate I was giving the patient acetarsone. It would be interesting to know which did him the most good.

PHILADELPHIA DERMATOLOGICAL SOCIETY

VAUGHN C. GARNER, M.D., *Secretary*

Jan. 17, 1936

HERBERT J. SMITH, M.D., *Chairman*

LUPUS ERYTHEMATOSUS. Presented by DR. JOSEPH V. KLAUDER.

H. M., a man aged 45, presents confluent erythematoscaly patches of twenty-three years' duration on the left side of the face and over the entire left ear, which is shrunken and atrophic. The scalp and mouth are normal.

DISCUSSION

DR. FRED D. WEIDMAN: I agree with the diagnosis. However, there are two other possibilities: lupus vulgaris erythematodes and porokeratosis of Mibelli. Casual inspection gives the impression that the margins of the lesions are elevated, but in my opinion analysis shows that their conspicuousness is due to the marked atrophy present in their central parts. By pressure I was not able to elicit anything that looked like the special focal infiltrations of tuberculosis. The location of the disorder around the ear calls to mind a patient whose case Dr. Corson reported and who was presented at two or more national meetings of dermatologists. That patient had an area of atrophy around the ear, extending thence over the scalp, and a diagnosis of possible granuloma annulare was made. I think that in that case eventually the disorder turned out to be porokeratosis of Mibelli. The reason I mention this is that one should be open minded in regard to lesions occurring around the ear and extending over the scalp and showing elevated margins. The eruption exhibited by Dr. Klauder's patient presents a degree of scaliness in the center which is not compatible with a diagnosis of porokeratosis of Mibelli.

DR. EDWARD F. CORSON: This patient undoubtedly has lupus erythematosus. I do not believe that the disorder closely suggests anything else. The patient to whom Dr. Weidman referred was presented about ten years ago at meetings of the American Dermatological Association and at the Atlantic Dermatological Conference and caused considerable discussion as to the diagnosis. Finally the diagnosis of sarcoid was agreed on. There is a picture in Andrews' textbook under the title of sarcoid which represents the nearest approach to the disorder in that particular case I have ever seen. At one of these meetings a wide range of diagnoses was offered. Dr. Gilchrist after looking at the sections thought that the disorder was epithelioma; Dr. Wise regarded it as granuloma annulare; some one else diagnosed it as serpiginous lupus vulgaris. No two members agreed on the same diagnosis.

DR. JOHN H. STOKES: Of late I have found it helpful to be highly suspicious of inflammatory processes that occur along the edge of the concha of the ear and down behind it. I think that a nickel dermatitis is one of the few new dermatologic diagnoses in recent years, and its association with pyogenic and seborrheic infections of the scalp, nose and ears sometimes produces pictures that are deceiving and easily overlooked. This combination of an inflammatory process around the ear and over the area of the nose which comes in contact with spectacles deserves to be looked into. I noticed that this patient has the mark of the bridge of spectacles over his nose. The possibility that the disorder may be due to the metal in the spectacles should be kept in mind even if the patient is not wearing spectacles at the time of examination or states that he does not use glasses, forgetting that he does when he reads.

A CASE FOR DIAGNOSIS. Presented by DR. H. J. GOLDMAN.

L. P., a Negress aged 39, states that about fifteen years ago nonpruritic papules developed on the left knee. They spread down the leg slowly but dis-

appeared completely after the patient received fifteen intravenous injections of a drug, the name of which she does not know. They were present for five years before this treatment was administered. After eight years they recurred on the left knee and spread to the extent seen at present. This second eruption is pruritic and greatly excoriated. It has been present for two years, having extended slowly. The general physical condition of the patient is normal.

A provocative test of the blood after injection of neoarsphenamine gave several negative Wassermann, Kahn and Eagle reactions. One test, however, showed a positive Eagle reaction. Several tests with various antigens made since have been negative. No examination of the spinal fluid has been made. A biopsy report from Dr. Weidman's laboratory stated that the pathologic picture was not that of syphilis, psoriasis or parapsoriasis. The patient received injections of neoarsphenamine totaling 1.2 Gm., which resulted in questionable improvement; one-half skin erythema dose of roentgen radiation brought about no change in the condition.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I suggest the diagnosis of syphilis.

DR. CARROLL S. WRIGHT: I think one ought to be able to rule out that diagnosis on the basis of the repeatedly negative reactions and the lack of response to antisyphilitic therapy. I believe that the disorder is a tuberculous process.

DR. JOHN H. STOKES: I could not decide what the lesion was, but I think that two other things should be considered: (1) ichthyosis hystrix and (2) a factitious eruption which the patient has maintained over a long period, not necessarily as a malingering performance but unconsciously as a minor traumatization. I think that these two things are worth including in the discussion, but frankly I can not decide what the disorder is.

DR. FRED D. WEIDMAN: The biopsy does not show anything that would indicate any particular dermatologic entity. One of the members informally mentioned lichen planus this evening, and because of the variable histologic picture which lichen planus may present, depending on its stage, I should say that in this case the histologic picture is more compatible with that than with tuberculosis or syphilis. There is no evidence of an important degree of cellular infiltration, and taking all the factors into consideration I think that the disorder resembles nontypical lichen planus more closely than it does any other disease. However, the distribution is not at all what one expects to see in lichen planus. When I first saw the patient I thought of certain conditions which Dr. Schamberg had seen, namely, a condition on the thighs of young men in which the infiltration is much more marked than that exhibited by Dr. Goldman's patient and in which areas of atrophy occur between the patches. One must remember the possibility of traumatism playing a part. The one case which I observed was in an athlete —a hurdler. I always believed that these apparently fibrosarcomatous lesions have a tuberculous basis, and as it is known that tuberculosis can produce a great range of changes it is possible that it may induce fibrous changes in the skin. I am inclined to regard this patient's disorder as atypical lichen planus, but I should like to hear more satisfactory suggestions.

ANTHRACOSIS OF THE SKIN. Presented by DR. PATRICIA DRANT.

H. K., a man, presents anthracotic markings on the left shin which appeared after application of activated charcoal in the treatment of a chronic ulcer of the leg. The ulcer is completely healed.

DISCUSSION

DR. FRED D. WEIDMAN: This patient was treated with activated charcoal over a period of many weeks in the Philadelphia General Hospital. The ulcer

was the size of a palm or larger when he first received that treatment, and I did not see him again until the entire lesion had become epitheliated. Then to my astonishment I noticed these linear anthracotic markings of the skin. They corresponded to the margins of the ulcer and my opinion is that portions of the charcoal became sequestered under the margins of the regenerating skin. This is a rather unusual illustration of another (therapeutically induced) method whereby anthracosis of the skin may develop. The disorder is known to appear on the faces and hands of miners, to follow injury with gunpower and to develop after a similar type of trauma. One should add activated charcoal to the list of substances that should not be applied to the skin therapeutically. This condition parallels those in which pigmentation of the face followed the use of lead subacetate in the treatment of ivy poisoning, the salt becoming reduced to metallic lead.

DR. SIGMUND S. GREENBAUM: Activated charcoal has a beneficial effect on some lesions. In this case no harm results from this type of pigmentation, as it is concealed from ordinary view and occurs in an aged subject. Of course, it would be extremely embarrassing in a woman or in a young person.

A CASE FOR DIAGNOSIS. Presented by DR. HERBERT J. SMITH.

E. C., a boy aged 10 years, presents a confluent acuminate follicular eruption involving the pilosebaceous orifices. It is inflammatory at times and is most marked on the extremities. In April 1934 the patient had German measles; the rash disappeared in one week, but the skin remained dry and rough. The patient had been healthy as a baby, and his skin had been normal until April 1934. When he was first seen, in July 1935, the keratosis was more marked than at present.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.: I think that in this case the age of the patient, the grouping of acuminate follicular papules, some of which are inflammatory and some of which contain small hairlike spines, and the fact that the eruption is especially marked on the extremities support a diagnosis of lichen spinulosus. When I first saw this patient about all I could do was to classify the disorder among the hypertrophies of the skin. I ruled out pityriasis rubra pilaris because of the absence of involvement of the scalp and nails and the absence of the characteristic spines over the fingers, and in my opinion the disorder is lichen spinulosus.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I agree with the diagnosis of lichen spinulosus.

DR. JOHN H. STOKES: I think there are several possibilities that should be further considered and more carefully investigated. One is lichen scrofulosorum. Occasionally it is associated with tuberculosis of the joints. A careful investigation for latent tuberculosis is indicated. The grouping which one sees in the ordinary lichen scrofulosorum is sometimes lacking. Another possibility is a dermatophytid. I have never forgotten the extremely unpleasant experience I had when Dr. Fred Harris found a dermatophytic process in the nails of a young girl with an eruption that strongly suggested pityriasis rubra pilaris. Removal of the finger-nails and cleaning the process about the nail beds caused the eruption to clear. In children these dermatophytids are occasionally the sequels of extremely small foci of dermatophytosis; therefore, careful search should be made, and one should not too readily despair if one does not find the organism the first time. The scalp particularly ought to be searched. Occasionally the dermatophytid long precedes the appearance of a kerion. The kerion suddenly appears on the scalp months after the child has shown the first signs of an almost exfoliative dermatitis. Moreover, some of the children with this disorder are extremely ill, showing toxic symptoms, elevation of temperature, and so on, before the focus of fungous infection is found. I also wish to call attention to the fact that over the front of the thorax this boy has something

besides follicular papules. He has the flat, more or less characteristic invisibly scaling papules of pityriasis lichenoides chronica. In some cases of parapsoriasis mixtures of types of lesions occasionally occur. At least three different types may appear in the same patient; hence I believe that the appearance on the front of the thorax of these flat, shiny papules which show no scale until they are abraded and then fluff up into a mass of scales is suggestive of that possibility. I think that a good deal of study of this boy's condition must be done before any of these diagnoses is accepted.

DR. FRED D. WEIDMAN: Some of the lesions show quite a good picture of lichen spinulosus, particularly if examined with a pocket lens. I am certain that the disorder is not pityriasis rubra pilaris. I believe, too, that there is something else on the skin besides the simple lichen spinulosus. What it is I do not know. I should like to make more investigations in respect to this other condition. At first I thought that possibly the additional lesions over the posterior part of the trunk and also over the upper parts of the chest were resolving eczematous lesions, but in one examination such as could be made tonight one cannot ascertain that. Resolving lesions of scabies may present an appearance similar to that exhibited by this patient; hence a great deal depends on the nature of the lesions of scabies in respect to the resolving lesions of eczema. One must have all the data before one can make a final pronouncement.

DR. JOHN H. STOKES: In my experience when an extensive follicular keratotic eruption is present one must also consider lichen planus. That may sound rather surprising, but in lichen planus there can be a range of lesions which one frequently forgets entirely, or one may forget that it is possible to have, in addition to typical flat angular shiny papules with pseudo-arsenical keratoses in the palms, keratosis pilaris, lichen spinulosus, and so on; and whenever lesions of lichen spinulosus appear the possibility of lichen planus should be considered in making the differential diagnosis.

INTERSTITIAL KERATITIS. Presented by DR. JOSEPH V. KLAUDER.

H. M., a girl aged 11 years, when first seen in November 1935 had interstitial keratitis involving the right eye of one week's duration. There was diffuse haziness of the entire cornea. The patient had received no treatment. With the site under local anaesthesia a piece of the cornea was excised; it was studied by the following methods: dark field examination, Levaditi's stain for spirochetes and intratesticular and intracorneal inoculation of rabbits. Spirochaeta pallida was not demonstrated by any of these methods. The rabbits were inoculated two months ago; hence they are still under observation.

INTERSTITIAL KERATITIS TREATED WITH QUININE BISULFATE WITHOUT EFFECT. Presented by DR. JOSEPH V. KLAUDER.

S. M., a girl aged 9 years, was first seen in October 1935, presenting severe interstitial keratitis involving both eyes. For two weeks she was given 2 grains (0.13 Gm.) of quinine bisulfate three times a day, without effect. Treatment with bismuth was then started and was effective. The patient has a peg-shaped tooth with a suggestion of a notched cutting surface. Quinine was administered by mouth in view of Schereschewsky's report (*Klin. Wchnschr.* **14:** 381, 1935) concerning the beneficial effect of quinine administered orally to patients with interstitial keratitis. Schereschewsky also reported a spirocheticidal effect of quinine in experimental syphilis in apes and in treatment of interstitial keratitis in syphilitic rabbits. In addition to employing quinine in the treatment of a patient with interstitial keratitis I studied the possible spirocheticidal action of the drug in syphilitic rabbits. It was observed that 20 mg. of quinine hydrochloride per kilogram of body weight administered intravenously was the lethal dose for rabbits. The animals survived an intravenous injection of 18 mg. per kilogram. An intravenous injection of 15 mg. per kilogram given to a rabbit with well pronounced testicular syphiloma

had no effect on the syphilitic lesion, as ascertained by dark field examination, or on the clinical course of the syphiloma.

INTERSTITIAL KERATITIS IN MOTHER AND CHILD (SYPHILIS IN THE THIRD GENERATION). Presented by DR. JOSEPH V. KLAUDER.

FIRST GENERATION.—The grandmother, aged 45, has a definite history of an eruption of secondary syphilis which occurred soon after her marriage. She received little treatment at the time; she had one miscarriage but no children born dead. She has one daughter. There were other siblings. The husband died of cancer. The Wasserman reaction of his blood was negative during the last illness. The woman showed no clinical evidence of syphilis. The Wassermann reaction of her blood was 11 —; the Meinicke reaction was 43.

SECOND GENERATION.—The daughter was aged 19 at the time of onset of bilateral interstitial keratitis. The clinical diagnosis was confirmed by examination with the slit lamp. There were no other stigmas of congenital syphilis. The Wassermann reaction was 444, and the Meinicke reaction, 44. She gave birth to one dead child and has one living daughter. The Wassermann reaction of her husband's blood was 444, and the Meinicke reaction, 44. This patient is now 25 years old. She was married at the age of 17.

THIRD GENERATION.—The granddaughter is 6½ years old; at the time of onset of interstitial keratitis she was 2½ years old. The examination with the slit lamp confirmed the clinical diagnosis. The Wassermann reaction was 4442, and the Meinicke reaction, 44. The luetin test was positive. Clinical examination gave essentially negative results except for the fact that one upper incisor is peg shaped; it is regarded as a Hutchinson tooth. There is a retinochoroiditis which is regarded as being of syphilitic origin.

DISCUSSION

DR. JOSEPH V. KLAUDER: The presence of a positive Wassermann reaction in the husband of the patient in the second generation complicates the interpretation. The grandmother asked me not to disclose the nature of the disease to her daughter and her husband; hence I could not question the husband regarding the source of infection. Did the husband infect his wife, in whom interstitial keratitis developed later? If so the woman presents a rare instance of interstitial keratitis in acquired syphilis. Granting that the wife has congenital syphilis, did she infect her husband? This is not likely. I believe that the positive Wassermann reaction of the husband's blood has no relation to his wife's infection but is purely coincidental. If one accepts interstitial keratitis as proof of congenital syphilis, then the child exhibits an instance of syphilis in the third generation. It is to be noted that the mother (second generation) had a typical interstitial keratitis at the age of 19 and that she was married at about the age of 17. This brings up the following important question: Does the early marriage of patients with congenital syphilis whose infection is untreated favor the transmission of the infection to their progeny? It is reasonable to believe that under these circumstances infection is more likely to be transmitted than if marriage is longer delayed.

DR. JOHN H. STOKES: I have no comment to make except that I think that this is a remarkable combination and that the evidence of syphilis in the third generation comes as close to being air tight as possible; much closer than in most cases. I think that there is a tendency to report cases as instances of syphilis in the third generation without adequate evidence, but that certainly is not the case in this presentation.

DR. SIGMUND S. GREENBAUM: I am glad that Dr. Klauder mentioned the possibility of the husband's superinfecting the wife. I have observed instances of superinfection in patients with congenital syphilis. In this presentation the extraordinary thing, I think, is the fact that both the mother and the child had interstitial keratitis—as though the cornea was the weak place in the make-up of each of these patients.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I have read an abstract in which an ointment containing a small amount of quinine was described as being used in treating interstitial keratitis. I also read an article recommending roentgen therapy to the cornea for the treatment of interstitial keratitis. Has Dr. Klauder used either of them?

DR. JOSEPH V. KLAUDER: I have used quinine locally in the treatment of interstitial keratitis too recently to draw any conclusions. I have never used roentgen therapy in treating that disease. I gather from the literature that the results were not sufficiently impressive to offset the risk inherent in roentgen radiation. The case in which I removed a piece of cornea is representative of a group of three cases in which a piece of cornea was removed but did not disclose S. pallida. This seems to indicate that the organism is not present at the site of the interstitial keratitis. The fact that interstitial keratitis may appear after fairly thorough treatment seems to me additional evidence against the hypothesis that the organisms are present in the cornea.

DR. JOHN H. STOKES: I have always believed that there was some doubt about the presence of the organisms in the cornea.

DR. JOSEPH V. KLAUDER: I inoculated the cornea as well as the testicles of a rabbit with spirochetes and obtained negative results. The rabbits are still under observation. The time since inoculation is about two months.

DR. FRED D. WEIDMAN: About the premises in interstitial keratitis I am not informed, but from analogy I should say that it would be unusual if S. pallida were to be demonstrated in interstitial keratitis. It is known how difficult it is to demonstrate the spirochetes even in active gumma, and in the other phases of syphilis, namely, in the diffuse fibrous one, it is even more difficult to recover the organism. I doubt, therefore, that these negative results of histologic studies or even of experimentation with rabbits indicate that the spirochetes are not present. The negative results merely show the well known difficulty of demonstrating the organisms in old syphilitic lesions.

DR. JOSEPH V. KLAUDER: The point is that all the methods used gave negative results—dark field examination, inoculation of animals and staining.

DR. SIGMUND S. GREENBAUM: I agree with Dr. Weidman. The negative results do not at all exclude the possibility of the organisms' being present. I have inoculated rabbits with many types of tissue and have obtained only negative results. The point is that those rabbits have to be watched over a period of four or five months before negative results can be reported.

A CASE FOR DIAGNOSIS. Presented by DR. JOSEPH V. KLAUDER.

I. K., a man aged 51, presents on the anterior aspect of the upper surface of the tongue an irregularly shaped ulcer 4 cm. long and 2 cm. wide with a yellowish surface and a raised undermined edge. There are confluent ulcerations on the tip and two ulcerations on the lower surface of the left side of the tongue. Clinically the condition is not malignant. No other dermatoses are present. The patient states that about two months before the ulcers appeared he had bitten his tongue. An ulcer appeared, which never entirely healed. The patient is undernourished; he has lost 10 pounds (4.5 Kg.) in six months. As he was seen for the first time today complete investigations have not been made.

DISCUSSION

DR. SIGMUND S. GREENBAUM: I suggest the diagnosis of tuberculous ulcers.

DR. FRED D. WEIDMAN: I think that some tissue should be stained for the organism if that has not been done.

DR. JOSEPH V. KLAUDER: It was done this afternoon.

DR. FRED D. WEIDMAN: Of course, it is in lesions of the mouth rather than in those of the pharynx or of the tongue that the organisms are found in cases of

superficial tuberculosis. They are much more commonly found there than on the skin proper. The patient exhibits a remarkably cleancut, punched-out ulcer. There is scarcely any infiltration, and the edges are not necrotic or shaggy. I thought that the necrotic tissue on the base of that ulcer was quite thin, so much so in fact that I thought I could make out the outlines of the architecture of the muscular tissue of the tongue underneath. There is little active tissue around that lesion. If such a condition were to occur on the skin I should say that the lesion was a type of trophic ulcer. I agree with Dr. Greenbaum, but I should be very chary of making a diagnosis of tuberculosis at this time. The patient ought to be examined neurologically to see whether there is any basis for the lack of reaction.

Dr. Sigmund S. Greenbaum: Of course when I suggested the diagnosis of tuberculosis I did not mean to make a diagnosis before the results of laboratory examination are reported.

Dr. Joseph V. Klauder: The biting of the tongue mentioned in the history apparently was slight. I do not believe that it is of any significance.

Pityriasis Rosea-Like Eruption Occurring During Bismuth Therapy. Presented by Dr. Thomas Butterworth, Reading, Pa.

D. B., a Negro aged 61, received twelve injections of bismuth subsalicylate, after which there appeared on the trunk an eruption consisting of oval, scaly and crusted lesions with their long axis along the lines of cleavage. The first patch appeared on the flexor aspect of the left elbow. The eruption appeared about Sept. 1, 1935, and changed little in the succeeding four months. During that time the bismuth therapy was continued. There is a bismuth line on the gums.

DISCUSSION

Dr. John H. Stokes: I am inclined to agree with Dr. Butterworth's diagnosis. It seems to me that the chronology makes it unlikely that the eruption is a manifestation of recurrent syphilis, of syphilis that is resistant to bismuth or of an infection which has appeared during the course of the bismuth therapy; hence I think that the interpretation of reaction to bismuth is probably correct. Some of the lesions seem somewhat more scaly than those resulting from bismuth therapy and look as if they showed some atrophic changes, possibly associated with some granulomatous infiltration. However, as the primary infection occurred so long ago and as there is no reason for regarding the infection as of a relapsing type or for considering the disorder a secondary eruption coming on in a period of bismuth activation or in spite of bismuth, I agree with the diagnosis.

Dr. Robert L. Gilman: I agree with the diagnosis.

Dr. Edward F. Corson: I wonder whether the lesion on the lip does not play some part in the symptomatology. While there is no information as to its features, it is possible that it may have been an initial lesion. The syphilis which is said to have been present before antedates the Wassermann test, and I am not sure that it can be proved that the patient had syphilis at that time. The lesions which he exhibits now are merely suggestive of a rupial type of syphilis. It is possible that the patient presents one of those rare instances of a second infection after a cure or that this is his first infection with the disease. The history is inadequate.

Dr. Thomas Butterworth, Reading, Pa.: Dark field examination of material from the granuloma which was present on the lip when the patient was seen showed no spirochetes. The lesion looked so much like an epithelioma that a biopsy was made. The pathologic report was nondescript. In the meantime the Wassermann reaction of the blood was reported to be positive, and the diagnosis of gumma was considered to be correct. In about three or four weeks the lesion involuted. The appearance of these cutaneous lesions brought up the question whether the disorder was pityriasis rosea complicating syphilis or whether the eruption was due to the

bismuth, and the treatment was continued much longer than the disorder warranted. The patient applied for treatment in September, and he was given bismuth whenever he came to the clinic. If the eruption recurs he will be presented again.

DR. H. J. GOLDMAN: The disorder at first examination suggested either epithelioma or syphilis. The patient was subjected to a therapeutic test with bismuth for three or four weeks, and the lesion involuted about 10 per cent. He has since received roentgen therapy, as a result of which the eruption has involuted.

DR. ROBERT L. GILMAN: I recall that the report on the biopsy stated that the lesion was of a nonspecific type, and at that time Dr. Butterworth and I thought that possibly the biopsy specimen did not really represent the growth. Rather than jeopardize the man further, however, we sent him to the radiotherapy department for treatment. I do not recall whether at the time we thought there was a bona fide epithelioma, but we thought there might be and considered it best to regard the lesion as such. I think that the syphilitic infection is indubitably of longer duration than six or seven months.

A CASE FOR DIAGNOSIS (DERMATITIS REPENS? DERMATOPHYTOSIS?). Presented by DR. CARROLL S. WRIGHT.

K. A., a woman aged 56, states that in December 1934 a "pus" infection developed around a heavy callosity on one sole. It gradually spread to involve the sole and the top of the foot, intense soreness and swelling resulting. The lesion was treated by the family physician with dyes and ointment containing salicylic acid, but no improvement resulted. The lesion failed to improve after application of wet dressings of boric acid, potassium permanganate and solution of aluminum acetate. It was intolerant to ointments except zinc oxide paste with no salicylic acid. At present the left foot is somewhat edematous. The dorsal surface is slightly reddened and crusted. The sole is almost entirely denuded of epithelium; it has a fungating appearance in certain areas, and in other areas it is eroded and crusted. There is no pustulation. The borders are scaling and undermined in places. A report on the laboratory examination stated that fungi had been found at one time but that none were demonstrable at present. Ordinary staphylococci were present; no yeasts were found. There was no sugar in the urine.

DISCUSSION

DR. CARROLL S. WRIGHT: The first time I saw this patient was in consultation with the family physician, who had been using an ointment containing a concentration of strong salicylic acid; the foot looked badly blistered and exhibited a good deal of pus. I regarded the lesion as an overtreated fungous infection and prescribed compresses of potassium permanganate and a simple paste containing boric acid. I have seen the patient only at rare intervals. On the first occasion I took some scrapings which disclosed no fungi, but a check-up was impossible.

DR. DAVID M. SIDLICK: There are many features about the disorder which suggest a late manifestation of syphilis. I understand that a serologic test has been negative, but I think that a thorough therapeutic test should be made.

DR. JOSEPH V. KLAUDER: I should not subscribe to the diagnosis of syphilis. I should consider the possibility of a malignant process and have a biopsy made. There is no outstanding condition that I have in mind as resembling this disorder.

DR. JOHN H. STOKES: First I thought of Madura foot, but later, under better lighting and in a somewhat altered position, I was impressed by the possible malignant aspect. It seems to me entirely possible that this patient has a diffuse carcinomatosis or sarcomatosis of the foot, which may have originated, as she describes it, in a chiropodist's tinkering with a lesion of some sort on the foot. It may have been a melanomatous growth. I have seen feet infiltrate without visible metastasis and become again half as big as they were originally from a nevus between the first and second toes which had been unnoticed. I should say that that

possibility is the most critical one in this case and calls for immediate biopsy. In my opinion syphilis would be the least likely possibility. An extensive fungous or fungous-pyogenic infection with cellulitis and elephantiasic change would be worth considering. One or two of the flat squamous lesions on the toes looked unusually like keratosis blennorrhagica, but one or two lesions do not justify a diagnosis. One might consider a pustular psoriasis and the resistant phenomenon—mycotic, pyogenic, whatever it may be—which Barber in England and Andrews in this country have described. The quicker this patient enters a hospital and has a specimen removed for biopsy, the sooner an accurate diagnosis will be reached.

DR. SIGMUND S. GREENBAUM: On the dorsum of the foot are small elevations suggestive of the lesions seen in cases of melanoma. I agree with Dr. Stokes that the most likely diagnosis is malignant degeneration.

DR. FRED D. WEIDMAN: I think that syphilis can be clinically excluded in this case. From the appearance of the foot one gets the impression that the process is proceeding from the center of the entire foot and enlarging it generally in all directions, as occurs in maduromycosis. Certainly the appearance of the sole and of the toes sticking out like big pegs in front—the foot evidently would not rest on the toes at all—bears out this impression. Of course, there is only the history to indicate that this remarkable enlargement has been present for two weeks. It may have been present for longer than that. In any event the progress of the lesion has been fast. I think that such rapid progress rather speaks against carcinoma; it reminds one more of sarcoma. And the type of the tissue—rather bright red—is more suggestive of sarcoma than of carcinoma. I think that a biopsy should be made and that roentgen examination should ascertain whether there is destruction of the osseous tissue in the interior of the foot. Exhaustive studies of the blood should be made; it is possible that the disorder is lymphoblastoma. I think it may turn out to be sarcoma; as a second possibility I should consider lymphoblastoma.

DR. CARROLL S. WRIGHT: I noticed the scar on the patient's lip the first time I saw her, and after leaving the house I discussed with the family physician the possibility of an old syphilitic infection, and he told me he had treated the patient for many years. I suggested that she be given more bismuth, but this was not done until I saw her again this fall. I gave her about six injections, and the foot has not improved. In fact, in the last week it has become much worse. Therefore I believe that the possibility of this lesion's being in any way related to a syphilitic process can be ruled out.

NOTE.—Scrapings showed no fungi. A biopsy showed a specific infectious granuloma on the order of tuberculosis. The pathologic diagnosis was possibly "frambesia."

INTERSTITIAL KERATITIS TREATED WITH MALARIA. Presented by DR. JOSEPH V. KLAUDER.

C. D., a youth aged 19, was first seen in February 1934, complaining of interstitial keratitis affecting the left eye. Malaria therapy was given, and he had ten consecutive rises of temperature to 106 F. He received no other treatment. There was a definite improvement in the interstitial keratitis. After this a few injections of a bismuth preparation were given. The patient then took a self-prescribed rest for two months. A short time later there was involvement of the right eye and still later a recurrence of the disorder in the left eye. The case demonstrates involvement of the second eye with interstitial keratitis and relapse in the first eye after malarial treatment of interstitial keratitis.

DISCUSSION

DR. JOHN H. STOKES: I wish to ask Dr. Klauder whether he has ever seen instances of malaria in congenitally syphilitic children precipitating interstitial keratitis?

DR. JOSEPH V. KLAUDER: No, I have not.

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

Regular Meeting, Jan. 23, 1936

EUGENE F. KELLEY, M.D., *President*

A CASE FOR DIAGNOSIS (SYPHILITIC ONYCHIA?). Presented by DR. SAMUEL FELDMAN.

J. F., a shoemaker aged 52, says that he is not aware of having a venereal disease. His wife had no miscarriages. The Wassermann and the Kahn reaction of the blood were 4 plus.

The nails show longitudinal ridges and irregular pitting. The edges are brittle and separated from the nail bed. The nail of the ring finger of the left hand shows a yellowish white area surrounded by a red rim, which is plainly visible through the healthy transparent portion of the nail plate. The entire area appears to be somewhat depressed below the surface of the nail and gives the impression of a circumscribed syphilitic papule. On the anterior surface of the left thigh there is a firm, painless swelling with a deep perforation in the center.

DISCUSSION

DR. ARTHUR SAYER: I believe that a diagnosis of syphilitic onychia cannot be made on purely clinical grounds; psoriasis, eczema and tinea must also be considered. The therapeutic test should settle the question of a syphilitic onychia.

DR. MARION B. SULZBERGER: I do not see how the therapeutic test can settle the diagnosis, since psoriasis and syphilis respond to the arsenical medication. I think that if the lesion on the leg is caused by syphilis it is in all probability a manifestation of tertiary syphilis, and it would be unusual to find lesions of the nails or syphilitic papules under the nails at the same time. The latter usually appear in early or in late stages of secondary syphilis. I agree that there is no pathognomonic picture of psoriasis of the nails except perhaps the typical psoriatic papule which is present underneath the nail. Jadassohn stated that the crescent-shaped subungual hyperkeratosis of the nail bed at both sides and near the free edge is a fairly characteristic manifestation of psoriasis of the nail, more so than stippling.

DR. ADOLPH ROSTENBERG: My conception of syphilitic onychia is that it is a dystrophic change. This patient presents a heaped-up lesion which fits more with the diagnosis of psoriasis or tinea than with that of syphilitic onychia.

DR. SAMUEL FELDMAN: I doubt that this patient's disorder is syphilitic onychia; that is why the diagnosis is presented with a question-mark. Heller described as a syphilitic papule of the nail bed a condition similar to that exhibited by this patient. Because of this similarity and of the associated gumma of the thigh and the positive Wassermann and Kahn reactions, the diagnosis of syphilitic onychia must be strongly considered.

A CASE FOR DIAGNOSIS (LICHEN PLANUS OF THE NAIL BED?). Presented by DR. MARION B. SULZBERGER.

M. W., a saleswoman aged 35, has suffered from diabetes mellitus for the past five or six years, requiring from 60 to 80 units of insulin daily. At present the diabetes is not entirely controlled by insulin and diet.

The eruption appeared on the dorsum of the right hand in the summer of 1933 and gradually spread to almost all parts of the body. When the patient was first seen, in July 1935, there was typical widespread lichen planus on the arms, legs, trunk and back. In addition, there were macerated whitish red plaques of lichen

planus about the anus and vulva. No lesions of the nails were noted. Topical applications were prescribed, and the patient was advised to have daily injections of solution of sodium arsenate.

When the patient was next seen, in January 1936, the cutaneous lesions were considerably improved, but the perianal and perivulvar lesions were unchanged. It was then noted that several nails on both hands were short and irregularly broken off. There was bluish subungual discoloration at the distal end of the affected nails beneath the broken nail plate.

DISCUSSION

DR. LOUIS CHARGIN: It is possible that the disorder is lichen planus of the nails. There is no reason that a nail affected with lichen planus may not appear as a spoon nail. In two cases which I observed recently, one of which was presented before this society (ARCH. DERMAT. & SYPH. **33**:1096 [June] 1936) there was no resemblance to the appearance of this patient's nails. Lichen planus of the nails develops slowly, whereas the involvement of the nails in this case has been rather rapid. There are no characteristic features of lichen planus of the nails. The diagnosis can be accepted if the lesions of the nails disappear simultaneously with the eruption of the body.

DR. MARION B. SULZBERGER: I agree with the remarks made by Dr. Chargin, but I wish to add some facts which were not brought out sufficiently in the history. This patient had widespread, disseminated typical lichen planus of the body when I first saw her in 1933. As a result of arsenical treatment and mild topical applications the condition cleared up sufficiently for the patient to forego further treatment until last week. At that time there was an exacerbation of lichen planus, and the patient claims that the lesions of the nails started to appear simultaneously with those of the skin. I do not know whether the disorder was discernible under the light tonight, but beneath the nails there are several discrete circumscribed papular and macular reddish blue discolorations. This feature and the history of the development of the lesions led me to believe that the disorder may be lichen planus of the nail bed.

DR. LOUIS CHARGIN: In the two cases of lichen planus of the nails which I observed the manifestations in the nails were associated with palmar lesions. The association is more than a mere coincidence. Cases of lichen planus of the palms and hence also of lichen planus of the nails are comparatively rare.

A CASE FOR DIAGNOSIS (MYCOSIS FUNGOIDES? LYMPHOBLASTOMA?). Presented by DR. H. B. FEILER.

C. K., a woman aged 35, presents a fairly generalized eruption of five months' duration. It is especially marked on the face, ears, trunk, arms and buttocks. The chest and abdomen are comparatively free from lesions. The eruption consists of confluent dusky red infiltrated patches, which include many areas of various sizes and patches of normal unaffected skin. The infiltration of the face is nodular. The dorsal aspects of both hands are studded with pea-sized yellowish nodules. The patient experiences difficulty in closing the hands.

There are marked loss of hair and erythema of the scalp but no visible infiltrations. There is no enlargement of the glands, though the inguinal glands are palpable. The liver is slightly enlarged, and the spleen is not palpable. The patient complains of severe itching and burning.

The blood count showed 72 per cent hemoglobin, 4,100,000 red cells and 34,900 white cells. The results of the differential count were as follows: polymorphonuclears, 48 per cent; monocytes, 2 per cent; eosinophils, 2 per cent; myelocytes, 2 per cent; normocytes, 1 per cent, and lymphocytes, 45 per cent.

Histologic examination showed that the stratum corneum was uniformly thin and nonnucleated. The epidermis was about eight cell layers thick, and there was a tendency toward flattening out of the rete pegs, obliterating the papillae of the corium. Scattered cells in the prickle cell layer showed intercellular edema with pyknosis of the nuclei. The intercellular bridges were uniformly distinct. The

entire corium in all its layers showed a diffuse increase in fibrous tissue and numerous collections of cells in foci, mainly perivascular. These collections of cells consisted of round cells, an occasional plasma cell and eosinophil and also large pale stellate cells of the reticular type. There was no indication that the cutaneous lesion had resulted from leukemic infiltration of the skin. The histologic picture was consistent with the diagnosis of mycosis fungoides.

DISCUSSION

DR. ARTHUR SAYER: I believe that the high white blood cell count, the moderate adenopathy and the infiltration on the face speak in favor of leukemia and against mycosis fungoides.

DR. DAVID BLOOM: The eruption on the extensor surfaces of the arms and on the trunk, with clearcut areas of healthy skin between violaceous infiltrated lesions, strongly suggests mycosis fungoides. However, the nodular eruption on the eyebrows and at the angles of the mouth presents the characteristic features of leukemia. The latter, together with the high leukocyte count and the lymphocytosis, suggest to me the diagnosis of leukemia in spite of the lack of adenopathy.

DR. WILBERT SACHS: Mycosis fungoides is one of the conditions which is included in the group of lymphoblastoma. It is not always possible to differentiate which entity it is. According to the biopsy, however, the disorder is not lymphatic leukemia. The histologic picture points more to mycosis fungoides.

DR. FRANK E. CROSS: It is known that in lymphoblastoma a biopsy of material from one part of the body may show mycosis fungoides while one of material from another area may show another form of lymphoblastoma. This patient's disorder may be one in which this combination exists. The picture does not suggest typical mycosis fungoides but rather leukemia.

DR. CLINTON H. MARTIN: The hard, drawn, thickened skin of the hands which almost suggests scleroderma of the palms and fingers would fit in more with the diagnosis of lymphoblastoma.

DR. MARION B. SULZBERGER: In reference to the histologic and the hematologic picture lymphatic leukemia has been mentioned. According to the hematologic report the disorder is not lymphatic leukemia but myeloblastic leukemia. Cutaneous lesions occur rarely in myeloblastic leukemia and when they do occur they often present a variegated appearance.

DR. ARTHUR SAYER: The point to be emphasized is that the patient suffers from lymphatic leukemia and yet the clinical picture looks like mycosis fungoides. This would be in agreement with Symmers (ARCH. DERMAT. & SYPH. **25**:1 [Jan.] 1932), who on the basis of many autopsies concluded that disorders diagnosed during life as mycosis fungoides were proved at autopsy to be Hodgkin's disease, leukemia or lymphosarcoma.

DR. PAUL GROSS: In speaking of leukemia one should be more specific. In this case the disorder is leukaemia cutis propria. The diffuse infiltration on the face is typical of that condition, and although the lesions on the arms and body are suggestive of mycosis fungoides, their symmetrical distribution and diffuse infiltration point to leukemia. It is by no means necessary for a typical leukemic blood picture to be present in early stages of primary leukemia of the skin, and the blood count in this case points only to a rapidly progressing leukemia of the lymphatic type. Clinically there is no evidence of myelogenous leukemia.

DR. LOUIS CHARGIN: This patient exhibits deep-seated infiltrations on the trunk with numerous clear areas, a picture which as a rule indicates mycosis fungoides. The section shows a multiplicity of cell types. Therefore, the clinical and the histologic picture fit in well with the diagnosis of mycosis fungoides. The face, however, shows infiltrations, a feature which is not seen in mycosis fungoides but

is observed in disorders belonging to the leukemia group. If the infiltrations on the face are to be considered lymphatic leukemia, the blood picture should corroborate the diagnosis. The blood picture in this case is not incompatible with, but is by no means typical of, lymphatic leukemia. Moreover, one would expect an adenopathy, and that is lacking. While this patient shows characteristics of two diseases, no one disease can be singled out. Perhaps this fits well with the point brought out by Dr. Sayer in respect to Symmer's studies.

Dr. Adolph Rostenberg: The condition may start clinically like mycosis fungoides and later assume the character of lymphosarcoma or leukemia. A case which I had the opportunity to observe exemplified the difficulty in diagnosis: The patient, whom I presented before this society, had large tumors suggesting melanomas, which, however, yielded rapidly to roentgen treatment. This led me to suspect leukemia. The blood picture, however, was entirely normal for eight months. Eventually the patient died. But shortly before death the blood picture became typical of lymphatic leukemia. In the patient presented tonight the lesions of the body look like mycosis fungoides. The lesions of the face fit in well with the picture of leukemia. I suggest roentgen treatment for diagnostic purposes.

Dr. Samuel M. Peck: Perhaps this subject is being complicated unnecessarily. The clinical appearance certainly suggests mycosis fungoides; histologically there is some basis for this diagnosis also. If one wishes to maintain that the lesions on the face are those of lymphatic leukemia, that assertion should be based on some histologic proof. In the presence of an atypical histologic picture the hematologic picture should be the basis of the diagnosis. A competent pathologist, such as Ludwig Pick, of Berlin, Germany, has often stated that histologically it is almost impossible to make a differential diagnosis between aleukemic leukemia and lymphosarcoma. There are, however, certain criteria which help to make a differential diagnosis between these conditions. In mycosis fungoides there is a marked polymorphous infiltration and large clear cells are present. In lymphosarcoma and aleukemic leukemia there is a monomorphous type of cellular infiltration. In lymphosarcoma the cutaneous lesions more closely resemble those of a lymph node than in aleukemic leukemia. I mean by that that there is a more definite stroma in addition to the cells. In my opinion there is no definite hematologic picture in mycosis fungoides. In this case I think that an examination of the blood should be made by a competent hematologist.

Dr. H. B. Feiler: The lesions on the face and hands are more infiltrated than in mycosis fungoides. The deeper infiltrations and the hematologic picture suggest lymphoblastoma.

Recklinghausen's Disease in a Negro Boy. Presented by Dr. Isidore M. Lashinsky.

This 7 year old Negro boy came to the Harlem diagnostic clinic of the Board of Health on Jan. 5, 1936, presenting tumors scattered over the body. His mother stated that the first tumor appeared on his back in the sacro-iliac region about four years ago. The patient, the elder of two children, was born normally at term. There is no history of consanguinity.

The patient is poorly nourished; he presents about one hundred tumors covering the trunk, extremities and face. The tumors are freely movable and skin colored, and the majority vary in size from that of a pea to that of a walnut. The largest tumor is situated in the sacro-iliac region and is the size of a lemon. Almost all the tumors are hard and tender to the touch; the largest is soft and lobulated and is not only tender but at times painful. There are definite café au lait spots on the right side of the chest below the axilla, on the posterior aspect of the right arm, on the right scapula, on the right thigh and on both buttocks. The child is mentally retarded.

Physical examination gave negative results. The urine was normal. The Wassermann reaction of the blood of the mother and of that of the child was negative.

Histologic examination confirmed the diagnosis of Recklinghausen's disease.

DISCUSSION

DR. LOUIS CHARGIN: The whole picture, including the large tumor, is that of Recklinghausen's disease.

DR. PAUL GROSS: The tumor on the back is extremely firm and large. Many of the smaller nodules present the same firmness. Although the clinical picture indicates Recklinghausen's disease, one should exclude the diagnosis of a more malignant growth, especially that of a neurogenic sarcoma.

DR. HARRY KEIL: Before the diagnosis of Recklinghausen's disease is accepted, that of fibrolipoma should be ruled out by biopsy. The large tumor on the back apparently consists of a number of nodules of about the same consistency as the discrete lesions. If the disorder is Recklinghausen's disease it is of the fibromatous type.

DR. MARION B. SULZBERGER: I have seen few cases of Recklinghausen's disease in Negro children. It seems to me that in this case the tumors are too hard to be lesions of Recklinghausen's disease; moreover, in no places are there any tabs or protruding soft tumors. The lesions lie beneath the skin and lack the usual herniation. Furthermore, while there are some pigmented nevi, one cannot class them with certainty as café au lait spots. The tumors in this case are tender and even painful; that is not the usual finding in Recklinghausen's disease. In addition to this, the large, hard tumor located on the back is distinctly lobulated, which is another unusual feature. Whether Recklinghausen's disease may take on this form in Negroes, I do not know, but I cannot subscribe to that diagnosis in this case without knowing the results of a histologic examination.

DR. HENRY SILVER: All the criteria necessary for a diagnosis of Recklinghausen's disease are present: the usual small and large tumors of various consistency, the larger pigmented spots and the spots which would be café au lait on a white skin but on Negro skin are necessarily darker. I agree with Dr. Gross that the large, firm tumor may be malignant. In rare instances malignant tumors have been observed in association with Recklinghausen's disease.

DR. SAMUEL FELDMAN: In some conditions diagnosed as Recklinghausen's disease there may be no other lesion than café au lait spots or there may be in addition one or two small tumors or nevi. There is no combination of lesions that is not possible in that disease. In a certain case one may see a large number of tumors of one type and an insignificant number of or no tumors of another type. As far as the size of the tumor is concerned, I wish to recall a case of Recklinghausen's disease in which the diagnosis was proved by histologic examination which I presented before this society several years ago; in that case there was a large tumor on the abdomen in addition to numerous small lesions.

DR. SAMUEL M. PECK: I wish to point out that several of the lesions which this patient presents are uncommon in ordinary Recklinghausen's disease. I am referring to the lesions in the supraclavicular region of the right side, which are freely movable hard nodules. In the broad sense Recklinghausen's disease shows a tendency to a certain type of nevoid formation which seems to be closely related to the nerves and pigmentary system. That is why neurofibromas and even melanomas are encountered. The tumors found in patients with Recklinghausen's disease are varied, and several types of tumor may be present in one patient.

DR. ISIDORE M. LASHINSKY: I do not doubt that malignant degeneration may occur in a case of Recklinghausen's disease, but the large tumor on the back has existed for four years, and in view of this it can hardly be regarded as malignant.

A CASE FOR DIAGNOSIS (URTICARIA PIGMENTOSA WITHOUT PIGMENTATION [PARKES WEBER]? PARAPSORIASIS [JULIUSBERG]?). Presented by DR. LOUIS CHARGIN.

I. A., a salesman aged 40, presents an eruption of eight months' duration. It appeared first on the sides of the trunk and later spread to other parts of the

body. The lesions are small reddish macules and have persisted since the onset of the disorder. There is no itching. The lesions do not urticate to any extent on irritation. There is practically no pigmentation.

DISCUSSION

DR. LOUIS CHARGIN: There are two points to be stressed: 1. The eruption clinically resembles urticaria pigmentosa, and yet there is little or no pigmentation and the lesions do not urticate. 2. Parapsoriasis must be considered as a possibility. Urticaria pigmentosa without pigmentation has been described under various names. I present this patient as exhibiting a disorder of the type described by Parkes Weber.

DR. THEODORE ROSENTHAL: I agree with the diagnosis of urticaria pigmentosa with or without pigmentation. Some of the lesions on the body appeared fairly well pigmented.

DR. SAMUEL FELDMAN: I could not see any pigmentation. However, the appearance of the lesions fits in with the picture of urticaria pigmentosa, and lesions of this type with slight pigmentation are not uncommon in that disease. I am inclined to accept a diagnosis of urticaria pigmentosa, although it is impossible to rule out parapsoriasis without a biopsy.

DR. DAVID BLOOM: In spite of the lack of pigmentation I am inclined to accept the diagnosis of urticaria pigmentosa. The eruption has been present for only eight months, and it is possible that pigmentation will appear later. In parapsoriasis the picture is quite different. The peculiar mottling and the psoriasiform lesions seen in parapsoriasis are absent in this case.

DR. ISIDORE M. LASHINSKY: About three years ago I presented before this society a patient with urticaria pigmentosa acquisita in whom the manifestations were identical to those exhibited by Dr. Chargin's patient. When the eruption first appeared the lesions were of the same hue as the ones in this patient, being erythematous and not pigmented, but they did urticate. However, I fully agree with the diagnosis of urticaria pigmentosa.

DR. ADOLPH ROSTENBERG: I agree with the diagnosis of urticaria pigmentosa. The only doubtful point is that in early stages of the disease there should be some urtication which this patient's lesions do not show.

DR. PAUL GROSS: It is difficult to make a diagnosis in view of the lack of pigmentation and the absence of a convincing urticarial reaction. On the other hand, there are small lichenoid papules on the flexor surface of the forearms and on the inner surface of the arms besides a few slightly scaly reddish macules which may point to the diagnosis of parapsoriasis.

DR. LOUIS CHARGIN: If the disorder were typical urticaria pigmentosa there would be no special reason for presenting the patient. The fact is that the lesions are not pigmented and do not urticate. In disorders of this type as described by F. Parkes Weber (*Brit. J. Dermat.* **42**:374, 1932) mast cells have been found, but thus far I have been unable to obtain material for a biopsy. There are some papules on the forearms, one or two of which show some scaliness, and it is that which suggests the possibility of parapsoriasis of the Juliusberg variety.

Directory of Dermatologic Societies *

INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY (CANADIAN BRANCH)

H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

H. W. Barber, President, 7, Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7, Devonshire Pl., London, W. 1.

NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Paul A. O'Leary, Chairman, 102 Second Ave., S.W., Rochester, Minn.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.

AMERICAN DERMATOLOGICAL ASSOCIATION

John H. Stokes, President, 3800 Chestnut St., Philadelphia.
F. D. Weidman, Secretary, University of Pennsylvania, Philadelphia.

SECTIONAL DERMATOLOGIC SOCIETIES

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cleveland. Time: Dec. 5, 1936.

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

Samuel Goldblatt, President, 3208 Colerain Ave., Ciscinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

Henry J. F. Wallhauser, President, Medical Tower, Newark.
Louis J. B. LeBel, Secretary, 165 Grant Ave., Nutley.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of January, March, May, September and November.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Jack W. Jones, Chairman, 384 Peachtree St., Atlanta, Ga.
Winston U. Rutledge, Secretary, 332 W. Broadway, Louisville, Ky.
Place: Baltimore. Time: Nov. 17-20, 1936.

STATE DERMATOLOGIC SOCIETIES

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY AND SYPHILOLOGY SECTION

Thomas J. Clark, Chairman, 400, 29th St., Oakland.
George V. Kulchar, Secretary, 450 Sutter St., San Francisco.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY

Maurice J. Strauss, Chairman, 41 Trumbull St., New Haven, Conn.
Edward A. Abbey, Secretary, 442 Temple St., New York.

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville.
W. M. Sams, Secretary, 310 Ingram Bldg., Miami.

LOUISIANA DERMATOLOGICAL SOCIETY

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harvey P. Towle, President, 453 Marlborough St., Boston.
Rudolf Jacoby, Secretary, 270 Commonwealth Ave., Boston.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Louis Tullipan, Chairman, 224 E. 17th St., New York.
C. H. Peachey, Secretary, 197 S. Goodman St., Rochester.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA SECTION ON DERMATOLOGY

Abraham Strauss, Chairman, Medical Arts Bldg., Philadelphia.
L. G. Bembauer, Secretary, 5026 Jenkins Arcade Bldg., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

A. E. Schiller, Chairman, 10 Peterboro St., Detroit.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

MINNESOTA DERMATOLOGICAL SOCIETY

L. H. Winer, President, 78 S. Ninth St., Minneapolis.
F. W. Lynch, Secretary, Lowry Medical Arts Bldg., St. Paul.
Time: First Wednesday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Charles P. Bondurant, President, 412 Medical Arts Bldg., Oklahoma City.
Darrell G. Duncan, Secretary, 914 Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

C. M. Griswold, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Galveston. Time: October.

LOCAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Dudley C. Smith, President, University of Virginia Hospital, Charlottesville, Va.
Francis A. Ellis, Secretary, 104 W. Madison St., Baltimore.

Bronx Dermatological Society

Paul Gross, Chairman, 35 E. 84th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Samuel Hecht, President, 679 Greene Ave., Brooklyn.
Mortimer J. Cantor, Secretary, 907 St. Marks Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl L. Eaton, President, 40 North St., Buffalo.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

Central New York Dermatological Society

George M. Fisher, President, 264 Genesee St., Utica.
Rudolph Ruedemann Jr., Secretary-Treasurer, 214 State St., Albany.

Chicago Dermatological Society

Max S. Wien, President, 104 S. Michigan Ave., Chicago.
Reuben Nomland, Secretary, 25 E. Washington St., Chicago.

Cincinnati Dermatological Society

Raymond G. Senour, President, Carew Tower, Cincinnati.
Leon Goldman, Secretary-Treasurer, Doctors Bldg., Cincinnati.

Cleveland Dermatological Society

John E. Rauschkolb, President, 1705 Medical Arts Bldg., Cleveland.
C. L. Cummer, Secretary, 1010 Hanna Bldg., Cleveland.

Detroit Dermatological Society

W. G. Wander, President, 509 Kresge Bldg., Detroit.
G. Warren Hyde, Secretary-Treasurer, 2501 W. Grand Blvd., Detroit.

Los Angeles Dermatological Society

Harry P. Jacobson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Thomas W. Nisbet, Secretary, 65 N. Madison Ave., Pasadena, Calif.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Isidore Rosen, Chairman, 106 E. 54th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrook St., E., Montreal, Canada.

New England Dermatological Society

William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

J. Gardner Hopkins, Chairman, 102 E. 78th St., New York.
David Bloom, Secretary, 135 E. 50th St., New York.

NEW YORK DERMATOLOGICAL SOCIETY

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

OMAHA DERMATOLOGICAL SOCIETY

J. A. Borghoff, Chairman, 1319 Medical Arts Bldg., Omaha.
Donald J. Wilson, Secretary, 1113 Medical Arts Bldg., Omaha.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Vaughn C. Garner, Chairman, Germantown Professional Bldg., Philadelphia.
Thomas Butterworth, Secretary, 238 N. 5th St., Reading, Pa.

PITTSBURGH DERMATOLOGICAL SOCIETY

Emerson Gillespie, President, 120 Tuscarawas St., Canton, Ohio.
Joseph J. Hecht, Secretary, 506 Medical Arts Bldg., Pittsburgh.

ST. LOUIS DERMATOLOGICAL SOCIETY

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: Second Wednesday of each month.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

L. R. Taussig, President, 384 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.